

10/743,449

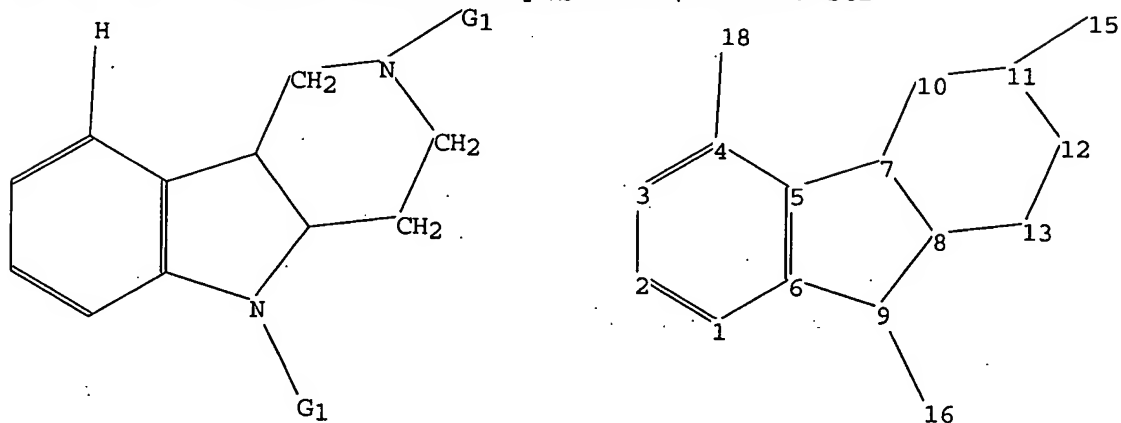
\* \* \* \* \* STN Columbus \* \* \* \* \*

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Uploading C:\Program Files\Stnexp\Queries\10743449.str



chain nodes :

15 16 18

ring nodes :

1 2 3 4 5 6 7 8 9 10 11 12 13

chain bonds :

4-18 9-16 11-15

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 7-10 8-9 8-13 10-11 11-12 12-13

exact/norm bonds :

6-9 8-9 9-16 11-15

exact bonds :

4-18 5-7 7-8 7-10 8-13 10-11 11-12 12-13

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6

isolated ring systems :

containing 1 :

G1:C,H

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom  
11:Atom 12:Atom 13:Atom 15:CLASS 16:CLASS 18:CLASS

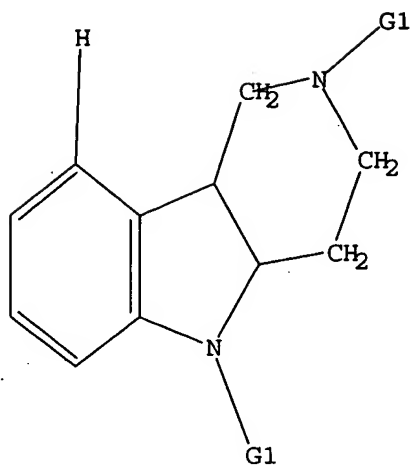
L1 STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1 STR

10/743,449



G1 C,H

Structure attributes must be viewed using STN Express query preparation.

=> s 11 full

L3 1026 SEA SSS FUL L1

=> file ca

=> s 13

L4 315 L3

=> s 5ht

L5 2702 5HT

=> s 14 and 15

L6 1 L4 AND L5

=> s 14 and (pharm? or drug?)

517571 PHARM?

719946 DRUG?

L7 149 L4 AND (PHARM? OR DRUG?)

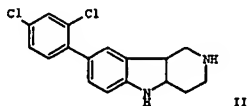
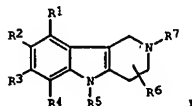
=> s 16 or 17

L8 150 L6 OR L7

=> d 16 ibib abs fhitstr

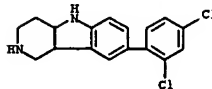
L6 ANSWER 1 OF 1 CA COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 138:170224 CA  
 TITLE: Preparation of 1H-pyrido[4,3-b]indoles as 5-HT receptor ligands  
 INVENTOR(S): Ennis, Michael D.; Frank, Kristine E.; Hoffman, Robert L.; Fu, Jian-Min  
 PATENT ASSIGNEE(S): Pharmacia & Upjohn Company, USA  
 SOURCE: PCT Int. Appl., 58 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003014118	A1	20030220	WO 2002-US25130	20020806
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, GR, HU, IL, IN, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GV, ML, MR, NE, SN, TD, TG				
CA 2453537	AA	20030220	CA 2002-2453537	20020806
US 2003060464	A1	20030327	US 2002-214405	20020806
US 6849640	B2	20050201		
EP 1414819	A1	20040506	EP 2002-757023	20020806
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
PRIORITY APPLN. INFO.: US 2001-310890P P 20010808 WO 2002-US25130 W 20020806				
OTHER SOURCE(S): MARPAT 138:170224 G1				



AB 2,3,4,4A,5,9b-hexahydro-1H-pyrido[4,3-b]indoles and 2,3,4,5-tetrahydro-1H-pyrido[4,3-b]indoles of formula I [R1-R4 = H, halo, CF3, OCF3, CN, NO2, alkyl, cycloalkyl, (substituted) OH, aryl, etc.]; R5 = H, alkyl, cycloalkyl, aryl, heteroaryl, etc.; R6 = H, alkyl; R7 = H, alkyl, alkenyl,

L6 ANSWER 1 OF 1 CA COPYRIGHT 2005 ACS on STN (Continued)  
 alkynyl, aryl, etc.] are prepd. These compds. are 5-HT ligands that are useful for treating diseases wherein modulation of 5-HT activity is desired. Thus, II was prepd. from 8-bromo-2,3,4,5-tetrahydro-1H-pyrido[4,3-b]indole and 2,4-dichlorophenyl boronic acid in 4 steps. The compds. displace >50% of a radiolabeled test ligand from 5-HT receptor subtypes at 1 µM concn.  
 IT RL: DGN (Diagnostic use); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (Preparation of pyridoindoles as 5-HT receptor ligands)  
 RN 497261-07-1 CA  
 CN 1H-Pyrido[4,3-b]indole, 8-(2,4-dichlorophenyl)-2,3,4,4a,5,9b-hexahydro-(9CI) (CA INDEX NAME)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

10/743,449

=> s 17 and py<2003

21763362 PY<2003

L9 134 L7 AND PY<2003

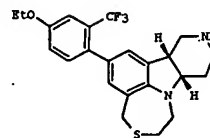
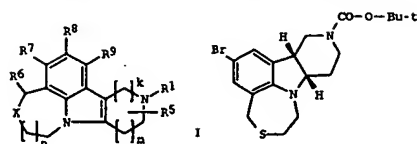
=> d ibib abs fhitr 1-50

L9 ANSWER 1 OF 134 CA COPYRIGHT 2005 ACS ON STN  
 ACCESSION NUMBER: 137:140432 CA  
 TITLE: Preparation of pyridoindoles as human serotonin  
 receptor 5-HT<sub>2C</sub> agonists and 5-HT<sub>2A</sub> antagonists  
 INVENTOR(S): Robichaud, Albert J.; Fevig, John M.; Mitchell, Ian  
 S.; Lee, Taekyu; Chan, Wenqing; Cacciola, Joseph  
 PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA  
 SOURCE: PCT Int. Appl., 409 pp.  
 CODEN: PIXKD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002059129	A2	20020801	WO 2001-US49371	20011219 <--
WO 2002059129	A3	20030130		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GR, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MY, NZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, EG, KE, KZ, MD, RU, TJ, TM, KW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2432185	AA	20020801	CA 2001-2432185	20011219 <--
EP 1343791	A2	20030917	EP 2001-994316	20011219
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
KE 200300296	A	20031215	KE 2003-296	20011219
JP 2005506281	T2	20050303	JP 2002-559431	20011219
BG 107865	A	20040730	BG 2003-107865	20030530
ZA 2003004305	A	20040902	ZA 2003-4305	20030602
NO 2003002797	A	20030819	NO 2003-2797	20030619
PRIORITY APPL. INFO.: US 2000-256740P P 20001220 WO 2001-US49371 W 20011219				
OTHER SOURCE(S): MARPAT 137:140432 GI				

L9 ANSWER 1 OF 134 CA COPYRIGHT 2005 ACS ON STN (Continued)

L9 ANSWER 1 OF 134 CA COPYRIGHT 2005 ACS ON STN (Continued)



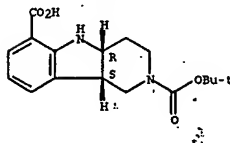
AB Title compds. I and their pharmaceutically acceptable salts [R<sup>1</sup> = H, alkyl, alkenyl, alkynyl, etc.; R<sup>5</sup>, R<sup>6</sup> = H, alkyl; R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup> = H, halo, CF<sub>3</sub>, aryl etc.; k, n = 1, 2; m = 0, 1; X = O, S, SO, etc.] and formulations were prepared. For example, Suzuki coupling of chiral bromide II, e.g., prepared in 7 steps from 1,5-dihydro-4,1-benzothiazepin-2(3H)-one, and 4-ethoxy-2-trifluoromethylphenyl boronic acid, followed by BOC deprotection afforded pyridoindole TFA III. In vitro radioligand binding assays, compds. I had IC<sub>50</sub> values < 50 nM for 5-HT<sub>2A</sub> antagonism or 5-HT<sub>2C</sub> agonism. Compds. I are useful in the control or prevention of central nervous system, sexual, gastrointestinal disorders etc..

II RL: RCT (Reactant); SPN (Synthetic preparation); PREF (Preparation); RACT (Reactant or reagent) (intermediate); preparation of pyridoindoles as human serotonin receptor 5-HT<sub>2C</sub> agonists and 5-HT<sub>2A</sub> antagonists

RN 444721-89-5 CA

CN 2H-Pyrido[4,3-b]indole-2,6-dicarboxylic acid, 1,3,4,4a,5,9b-hexahydro-, 2-(1,1-dimethylethyl) ester, (4aR,9bS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L9 ANSWER 2 OF 134 CA COPYRIGHT 2005 ACS ON STN  
 ACCESSION NUMBER: 135:267165 CA  
 TITLE: Stobadine protects isoproterenol-induced toxic damage in rats  
 AUTHOR(S): Macickova, Tatiana; Navarova, Jana  
 CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, SK-84216, Slovakia  
 SOURCE: Biologia (Bratislava) (2000), 55(Suppl. 8), 69-73  
 CODEN: BLOAOO; ISSN: 0006-3088  
 PUBLISHER: Slovak Academy of Sciences  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

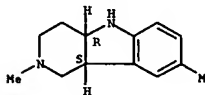
AB The pyridoindole stobadine (STO) is an effective cardioprotective drug with oxygen free radical scavenging properties. Isoproterenol (IPN), a synthetic catecholamine, is capable to induce massive myocardial necrosis accompanied with lysosomal enzyme (LE) activity changes in most mammals, when administered in high doses. The present study investigated the ability of STO to protect exptl. animals against IPN-induced toxic damage. The activities of the lysosomal enzymes cathepsin D and N-acetyl-β-D-glucosaminidase were studied in the rat heart as markers of cell damage. Male Wistar rats weighing 280-300g were used for these expts. IPN-induced toxic damage in rats (9 h after mg.kg<sup>-1</sup> s.c.) was manifested by marked alterations in the activities of LE in the sedimentable fraction of the rat myocardium. STO administered in various dosage regimens reduced or eliminated the IPN-induced biochem. changes in the rat myocardium. From the results presented in this study we conclude that STO is able to protect rats against IPN-induced toxic damage.

II RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (stobadine protects against isoproterenol-induced toxic damage in rats)

RN 85202-17-1 CA

CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)- (9CI) (CA INDEX NAME)

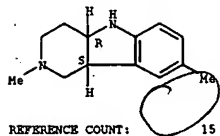
Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 134 CA COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 135:267164 CA  
 TITLE: Effects of stobadine on hypoxia and hypoxia/reoxygenation injury in isolated hepatocytes from fasted rats  
 AUTHOR(S): Berek, Stefan; Juranek, Ivo  
 CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, SK-84216, Slovakia  
 SOURCE: Biologia (Bratislava) (2000), 55(Suppl. 8), 15-18  
 CODEN: BLOAAO; ISSN: 0006-3088  
 PUBLISHER: Slovak Academy of Sciences  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Cell injury due to hypoxia and reoxygenation was investigated in the system of parenchymal hepatocytes isolated from fasted rats. The functional and structural integrity of hepatocytes in hypoxia was evaluated on the basis of protein synthesis and [<sup>3</sup>H] release from prelabeled hepatocytes. Incubation of hepatocytes in nitrogen atmosphere resulted in significant inhibition of incorporation of [<sup>14</sup>C]-valine into hepatocyte protein. Treatment of hepatocytes in hypoxia with the antioxidant stobadine (0.1, 1.0 and 10.0 μM) reversed protein synthesis almost to control values. No changes were observed in [<sup>3</sup>H] release from prelabeled hepatocytes. In the experiment with hypoxia/reoxygenation, hepatocytes were exposed to 60 min hypoxia followed by 120 min reoxygenation and the injury was evaluated by lactate dehydrogenase (LD) leakage and formation of thiobarbituric acid reactive substances (TBARS). The addition of stobadine at the given concns. (0.1, 1.0 and 10.0 μM) before the onset of hypoxia resulted in dose dependent protection from hypoxia/reoxygenation injury of isolated hepatocytes.  
 IT 85202-17-1, Stobadine  
 RI: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (effects of stobadine on hypoxia and hypoxia/reoxygenation injury in isolated hepatocytes from fasted rats)  
 RN 85202-17-1 CA  
 CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

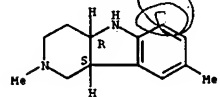


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THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 5 OF 134 CA COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 135:221089 CA  
 TITLE: Antiradical activity of some antilucer and local anesthetic active substances  
 AUTHOR(S): Dovollil, J.; Benes, Ludek  
 CORPORATE SOURCE: Ustav Chem. Leciv, Farm. Fak., Vet. a Farm. Univ., Brno, 612 42, Czech Rep.  
 SOURCE: Ceska a Slovenska Farmacie (2001), 50(4), 203-205  
 CODEN: CSLEPK; ISSN: 1210-7816  
 PUBLISHER: Ceska Lekarska Spolecnost J. Ev. Purkyne  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Czech  
 AB The in vitro free radical scavenging effects of 15 pharmacol. agents were examined by the the diphenyl-p-picrylhydrazyl assay (decrease in absorbance). Methylpentacainium iodide, mannitol, ascorbic acid, and HCl forms of pentacaine (K-1902), K-1904, K-1905, K-1906, K-1908, K-1909, K-1913, P-18, P-20, carbisocaine, lidocaine, stobadine were tested. A pronounced antiradical activity was observed with trapencaine, more than with stobadine, ascorbate, and mannitol. Trapencaine derivs. and lidocaine were less effective in comparison with trapencaine. The methylene group in the hydrophilic moiety of the trapencaine mol. (stereoisomers P-18 and P-20) led to the loss of antiradical activity, but the cis-isomer was more effective than the trans-isomer. The data suggest relationships of the chemical structure and antiradical and gastric cytoprotective activities.  
 IT 95751-51-2, Stobadine dihydrochloride  
 RI: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (antiradical activity of 15 antilucer and local anesthetic agents in vitro)  
 RN 95751-51-2 CA  
 CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, dihydrochloride, (4aR,9bS)-(9CI) (CA INDEX NAME)

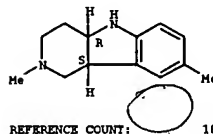
Absolute stereochemistry. Rotation (-).



● 2 HCl

L9 ANSWER 4 OF 134 CA COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 135:266992 CA  
 TITLE: Effect of stobadine on superoxide generation and degranulation of stimulated human polymorphonuclear leukocytes in vitro  
 AUTHOR(S): Pecivova, Jana; Macickova, Tatiana; Nosal, Rado; Danhelova, Edita  
 CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, SK-84216, Slovakia  
 SOURCE: Biologia (Bratislava) (2000), 55(Suppl. 8), 103-106  
 CODEN: BLOAAO; ISSN: 0006-3088  
 PUBLISHER: Slovak Academy of Sciences  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The authors studied the effect of stobadine, a pyridoindole antioxidant agent, on superoxide anion (O<sub>2</sub><sup>-</sup>) generation (respiratory burst) and enzyme (lysozyme and myeloperoxidase) release from FMLP (a specific receptor activator) and from PMA (activator of protein kinase C) stimulated human polymorphonuclear leukocytes (PMNL). Stobadine (1, 10, and 100 μM) decreased O<sub>2</sub><sup>-</sup> generation in FMLP stimulated PMNL only. It had no effect on enzyme release. The stobadine effect on O<sub>2</sub><sup>-</sup> generation seems to be linked to signal transduction rather than to its free radical scavenging and antioxidant properties since there was no effect on O<sub>2</sub><sup>-</sup> generation in PMA stimulated PMNL.  
 IT 85202-17-1, Stobadine  
 RI: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (stobadine on superoxide generation and degranulation of stimulated human polymorphonuclear leukocytes in vitro)  
 RN 85202-17-1 CA  
 CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

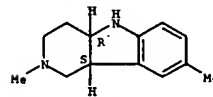


REFERENCE COUNT: 18

THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 6 OF 134 CA COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 135:189681 CA  
 TITLE: Placental transfer of the antioxidant stobadine at different gestational stages in rabbits  
 AUTHOR(S): Ujhazy, E.; Dubovicky, M.; Faberova, V.; Zemanek, M.; Soltes, L.; Gajdosik, A.; Ebyl, V.  
 CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, Slovakia  
 SOURCE: Methods and Findings in Experimental and Clinical Pharmacology (2000), 22(9), 683-688  
 CODEN: MFEPMK; ISSN: 0379-0355  
 PUBLISHER: Frous Science  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The distribution of [<sup>3</sup>H]-stobadine, a pyridoindole antioxidant, was investigated in New Zealand white rabbits and their fetuses on days 20 and 27 of gestation. The concns. of [<sup>3</sup>H]-stobadine were determined in maternal and fetal organs after oral administration in a single dose of 5.0 mg/kg. The results of the study showed that during the late period of gestation the fetal organs, especially the brain and heart, were under the protective action of the antioxidant stobadine.  
 IT 85202-17-1, Stobadine  
 RI: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (placental transfer of antioxidant stobadine at different gestational stages in rabbits)  
 RN 85202-17-1 CA  
 CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 34

THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 134 CA COPYRIGHT 2005 ACS ON STN

ACCESSION NUMBER:

135:61175 CA

TITLE:

Study of the kinetics of hydrolysis of stobadine acyl derivatives, the prodrug forms of extinguishers of free oxygen radicals. Part 3. Hydrolysis in neutral medium

AUTHOR(S):

Ondrasova, Miriam; Stankovicova, M.; Bezakova, Z.; Benes, L.

CORPORATE SOURCE:

Katedra Farm. Chem., Farm. Fak., Univ. Komenského, Bratislava, 832 32, Slovakia

SOURCE:

Ceska a Slovenska Farmacie (2003), 50(2), 86-91

PUBLISHER:

CODEN: CSLFEK; ISSN: 1210-7816

DOCUMENT TYPE:

Ceska Lekarska Spolecnost J. Ev. Purkyně

LANGUAGE:

Slovak

AB The pyridoindole derivative stobadine, [(-)-cis-2,8-dimethyl-2,3,4,4a,5,9b-hexahydro-1H-pyrido[4,3b]-indole] is a perspective antiarrhythmic, antihistamine, anesthetic, antilucous drug capable of extinguishing free oxygen radical. Its prodrug forms-N(5)-acyl-substituted stobadine - of the active substance - stobadine - have been prepared and it is assumed that the will be hydrolyzed in the organism and the active substance will be released in higher concns. in different biol. tissues. The present paper is concerned with the investigation of the kinetics of the hydrolysis of 13 acyl derivs. of stobadine in the medium of a buffer solution of pH 7 at temps. of 70°C and 75°C spectrophotometrically in the UV region of the spectrum. The determined

rate consts. were correlated with the length of the side acyl chain and the pKa values of the drugs under study. The profile of log k-pH of substances was determined

IT 154853-56-2

RL: PEP (Physical, engineering or chemical process); RCT (Reactant); PROC (Process); RACT (Reactant or reagent)  
(kinetics of hydrolysis of stobadine acyl derivs., the prodrug forms of extinguishers of free oxygen radicals)

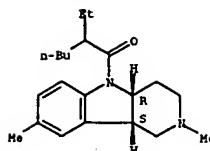
RN 154853-56-2 CA

CN 1H-Pyrido[4,3-b]indole, 5-(2-ethyl-1-oxohexyl)-2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, monohydrochloride, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L9 ANSWER 7 OF 134 CA COPYRIGHT 2005 ACS ON STN

(Continued)



● HCl

L9 ANSWER 8 OF 134 CA COPYRIGHT 2005 ACS ON STN

ACCESSION NUMBER:

134:35257 CA

TITLE:

Effect of dietary supplementation with the pyridoindole antioxidant stobadine on antioxidant state and ultrastructure of diabetic rat myocardium. Stefek, M.; Sotnikova, R.; Okruhlicova, L.; Volkovova, K.; Kucharska, J.; Gajdosik, A.; Gajdosikova, A.; Mihalova, D.; Hozova, R.; Tribulova, N.; Gvozdzakova, A.

CORPORATE SOURCE:

Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, 842 16, Slovakia

SOURCE:

Acta Diabetologica (2000), 37(3), 111-117

PUBLISHER:

CODEN: ACDAEZ; ISSN: 0940-5429

DOCUMENT TYPE:

Springer-Verlag

LANGUAGE:

Journal

AB Consistent with the postulated role of oxidative stress in the etiol. of late diabetic complications, pharmacol. interventions based on biol. antioxidants have been suggested. The aim of the present study was to investigate the effect of dietary supplementation with the pyridoindole antioxidant stobadine on the myocardial antioxidant status and ultrastructure of streptozotocin-diabetic rats. Diabetic male Wistar rats were fed for 32 wk a standard diet or a diet supplemented with stobadine (0.05% weight/weight). Control rats received a standard diet or stobadine-supplemented diet (0.16% weight/weight). Plasma levels of

glucose, cholesterol and triglycerides were increased significantly by diabetes. Activities of superoxide dismutase and catalase were markedly elevated in the diabetic myocardium. Myocardial levels of conjugated dienes increased after eight months of diabetes, in spite of significantly increased myocardial  $\alpha$ -tocopherol and coenzyme Q9 content. The long-term treatment of diabetic animals with stobadine (i) reduced plasma cholesterol and triglyceride levels yet left the severe hyperglycemia unaffected, (ii) reduced oxidative damage of myocardial tissue as measured by conjugated dienes, (iii) reversed myocardial levels of  $\alpha$ -tocopherol and coenzyme Q9 to near control values, (iv) reduced elevated activity of superoxide dismutase in the diabetic myocardium, and (v) attenuated angiopathic and atherogenic processes in the myocardium as assessed by electron microscopy examination. These results are in accordance with the postulated prooxidant role of chronic hyperglycemia and provide further evidence that development of pathol. changes in diabetic myocardium is amenable to pharmacol. intervention by biol. antioxidants.

IT 85202-17-1, Stobadine  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(effect of stobadine supplementation on antioxidant state and ultrastructure of diabetic rat heart)

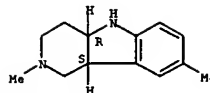
RN 85202-17-1 CA

CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L9 ANSWER 8 OF 134 CA COPYRIGHT 2005 ACS ON STN

(Continued)



REFERENCE COUNT:

65

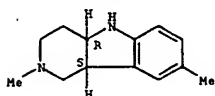
THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

19 ANSWER 9 OF 134 CA COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 134:336126 CA  
 TITLE: Preventive effect of several antioxidants after oxidative stress on rat brain homogenates  
 AUTHOR(S): Horakova, L.; Ondrejickova, O.; Bachrata, K.; Vajdova, M.  
 CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, 842 16, Slovakia  
 SOURCE: General Physiology and Biophysics (2000), 19(2), 195-205  
 CODEN: GPBIE2; ISSN: 0231-5882  
 PUBLISHER: Institute of Molecular Physiology and Genetics, Slovak Academy of Sciences  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Brain homogenate was used as a model system to study antioxidant properties of several natural and synthetic antioxidants under oxidative stress. Oxidative stress was induced by Fe/ascorbate system and lipid peroxidation, as well as protein modification were studied. Thiobarbituric acid reactive substances (TBARS) were used as a marker of lipid peroxidation. The preventive effect concerning lipid peroxidation decreased in the order: butylated hydroxytoluene (BHT) (3.5), stobadine (ST) (35), serotonin (54), trolox (98), U 74399G (160), melatonin (3100), (the nos. in the brackets represent IC50 in µmol/l). Methylprednisolone had no effect, and spin traps interfered with TBARS determination. Concerning creatine kinase (CK) activity as a selected marker of oxidative modification of proteins, the preventive effect of antioxidants (30 µmol/l) decreased in the order: BHT (30), trolox (75), stobadine (ST) (77), α-phenyl-N-tert-butyl-nitron (PEN) (87), sodium salt of N-tert-butyl-N-(phenyl-2-sulfone) nitron (SPEN) (90), (the nos. in the brackets represent the loss of CK activity in percentages, when 100 % was the loss of CK activity in the absence of any antioxidant). The nonglucocorticoid steroid U 74399G, methylprednisolone, and serotonin had no preventive effects, while melatonin had antioxidant effect only in a higher concentration (1 mmol/l).

IT 85202-17-1, Stobadine  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (preventive effect of antioxidants after oxidative stress in brain)  
 RN 85202-17-1 CA  
 CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)-(9CI) (CA INDEX NAME)

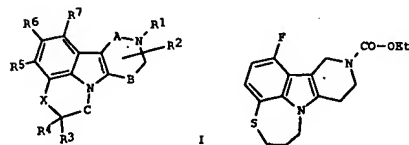
Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

19 ANSWER 10 OF 134 CA COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 134:56655 CA  
 TITLE: Preparation of substituted heterocycle fused gamma-carbolines  
 INVENTOR(S): Robichaud, Albert J.; Lee, Taekyu; Deng, Wei; Mitchell, Ian S.; Yang, Michael Guang; Haydar, Simon; Chen, Wenting; McClung, Christopher D.; Calvello, Emilio J. B.; Zawrotny, David M.  
 PATENT ASSIGNEE(S): Du Pont Pharmaceuticals Company, USA  
 SOURCE: PCT Int. Appl., 308 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 5  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000077002	A1	20001221	WO 2000-US16498	20000615 <--
W: AU, BR, CA, CN, CZ, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, UA, VN, ZA				
CA 2374239	AA	20001221	CA 2000-2374239	20000615 <--
EP 1189904	A1	20020327	EP 2000-941453	20000615 <--
EP 1189904	B1	20040922		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, NO				
BR 2000012086	A	20020402	BR 2000-12086	20000615 <--
TR 200103658	T2	20020621	TR-2001-200103658	20000615 <--
JP 2003502331	T2	20030121	JP 2001-503860	20000615
NZ 516031	A	20031031	NZ 2000-516031	20000615
US 6713471	B1	20040330	US 2000-594954	20000615
AT 277048	E	20041015	AT 2000-941453	20000615
ES 2223536	T3	20050301	ES-2000-942807	20000615
ES 2223537	T3	20050301	ES 2000-942808	20000615
ZA 2001009735	A	20040127	ZA 2001-9735	20011127
NO 2001006116	A	20020211	NO 2001-6116	20011214 <--
PRIORITY APPL. INFO.:			US 1999-139321P	P 19990615
			WO 2000-US16498	W 20000615
OTHER SOURCE(S):		MARPAT 134:56655		
GI				



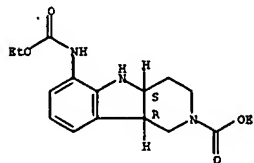
AB Novel γ-carboline compds. of formula I [R1, R2 = H, acyl, alkyl, cycloalkyl, etc.; R3, R4 = H, OH, amino, CF3, alkyl, etc.; R5-R7 = H,

19 ANSWER 9 OF 134 CA COPYRIGHT 2005 ACS on STN (Continued)

19 ANSWER 10 OF 134 CA COPYRIGHT 2005 ACS on STN (Continued)  
 halo, CF3, OH, CN, alkyl, aryl, heterocycle, etc.; X = (substituted) NH, (substituted) CONH, (substituted) NHCO, S; A, B, C = (CH2)n, n = 0-3] are prepd. The invention is also concerned with pharmaceutical formulations comprising these novel compds. as active ingredients and the use of the novel compds. and their formulations in the treatment of certain disorders. The compds. of this invention are serotonin agonists and antagonists and are useful in the control or prevention of central nervous system disorders including obesity, anxiety, depression, psychosis, schizophrenia, sleep disorders, sexual disorders, migraine, conditions assoc. with cephalic pain, social phobias, and gastrointestinal disorders such as dysfunction of the gastrointestinal tract motility (no data). Thus, II is prepd. starting from p-fluorothiophenol, β-propiolactone and 1-carbethoxy-4-piperidone. Pharmaceutical compns. contg. I are described.

IT 313369-59-4P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (preparation of substituted heterocycle fused γ-carbolines as serotonin agonists and antagonists)  
 RN 313369-59-4 CA  
 CN 2H-Pyrido[4,3-b]indole-2-carboxylic acid, 6-[(ethoxycarbonyl)amino]-1,3,4,4a,5,9b-hexahydro-, ethyl ester, (4aR,9bS)-rac- (9CI) (CA INDEX NAME)

Relative stereochemistry.

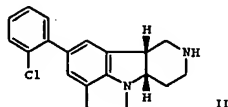
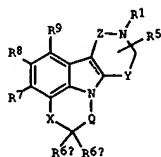


REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT



LS ANSWER 11 OF 134 CA COPYRIGHT 2005 ACS ON STN  
 ACCESSION NUMBER: 134:56654 CA  
 TITLE: Preparation of substituted heterocyclo  
 y-carbolines as serotonin agents  
 INVENTOR(S): Robichaud, Albert J.; Lee, Taekyu; Deng, Wei;  
 Mitchell, Ian S.; Chen, Wenting; McClung, Christopher  
 D.; Calvello, Emilie J. B.; Zavorotny, David M.  
 Du Pont Pharmaceuticals Company, USA  
 PATENT ASSIGNEE(S):  
 SOURCE: PCT Int. Appl., 388 pp.  
 CODEN: PIXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 5  
 PATENT INFORMATION:

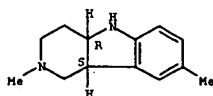
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000077001	A1	20001221	WO 2000-US16375	20000615 <--
W: AU, BR, CA, CN, CZ, EE, HU, IL, IN, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, TR, UA, VN, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2381322	AA	20001221	CA 2000-2381322	20000615 <--
EP 1189905	A1	20020327	EP 2000-94208	20000615 <--
EP 1189905	B1	20040329		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000012084	A	20020402	BR 2000-12084	20000615 <--
TR 200103658	T2	20020621	TR 2001-200103658	20000615 <--
JP 2003502330	T2	20030121	JP 2001-503859	20000615
US 6713471	B1	20040330	US 2000-594954	20000615
AT 277928	E	20041015	AT 2000-94208	20000615
ES 2223536	T3	20050301	ES 2000-94207	20000615
ES 2223537	T3	20050301	ES 2000-94208	20000615
ZA 2001009735	A	20040127	ZA 2001-9735	20011127
NO 2001006115	A	20020212	NO 2001-6115	20011214 <--
PRIORITY APPL. INFO.:			US 1999-139321P	P 19990615
			WO 2000-US16375	W 20000615
OTHER SOURCE(S):		MARPAT 134:56654		
G1				



AB The title compds. I (R1 = acyl, alkyl, alkenyl, alkynyl, cycloalkyl, etc.)

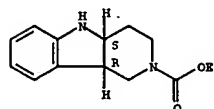
LS ANSWER 12 OF 134 CA COPYRIGHT 2005 ACS ON STN  
 ACCESSION NUMBER: 133:313480 CA  
 TITLE: Study of the kinetics of hydrolysis of stobadine acyl derivatives, prodrug forms of scavengers of free oxygen radicals. Part 2: Alkaline hydrolysis  
 AUTHOR(S): Ondrasova, M.; Stankovicova, Maria; Bezakova, Z.; Benes, L.  
 CORPORATE SOURCE: Katedra Farm. Chemie, Farm. Fakulta, Univ. Komenského, Bratislava, 832 32, Slovakia  
 SOURCE: Ceska a Slovenska Farmacie (2000), 49(5), 251-255  
 CODEN: CSLFEE; ISSN: 1210-7816  
 PUBLISHER: Ceska Lekarska Spolecnost J. Ev. Purkyne  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Slovak  
 AB Stobadine is a potential antiarrhythmic, antihistaminic, anesthetic, and antiulcer pharmacol agent with marked antioxidant effects. Stobadine NS acyl substitution yielded derivs., which represent prodrug forms of the active agent stobadine. They acyl derivs. may be hydrolyzed in the body and the active agent may be released in higher concns. in various target biol. tissues. The hydrolysis kinetics of 12 stobadine acyl derivs. was studied in 0.1 M NaOH at 70°C, using UV spectrophotometry. The hydrolysis rate consts. were correlated with the length of the acyl side-chain and the pKa values of the particular compds.  
 IT 85202-17-1B, Stobadine, acyl derivs.  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (stobadine acyl derivs. alkaline hydrolysis as model of release of free oxygen radical scavengers from prodrugs and its kinetics)  
 RN 85202-17-1 CA  
 CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



LS ANSWER 11 OF 134 CA COPYRIGHT 2005 ACS ON STN (Continued)  
 R5 = H, alkyl; R6a, R6b = H, OH, amino, CF3, alkyl, alkenyl, alkynyl, alkoxy, haloalkyl, cycloalkyl, aryl; R7 and R9 = H, halo, CF3, OH, cyano, NO2, amino, alkyl, alkenyl, alkynyl, cycloalkyl, haloalkyl, etc.; R8 = H, halo, CF3, CF3O, OH, NO2, cycloalkyl, alkyl, alkenyl, alkynyl, haloalkyl, alkoxy, haloalkoxy, etc.; X = CO, CH2, alkylmethylene, alkenylmethylene, alkynylmethylene, alkoxyethylene, alkoxyethylene; Q = (CH2)n, n = 0, 1, 2, 3; Y = (CH2)m, m = 0, 1, 2; Z = (CH2)q, q = 1, 2) and their pharmaceutically acceptable salt salts were prep'd. Thus, 1-amino-2,3-dihydroindole was treated with 4-piperidone HCl to give 4,5,7,8,9,10-hexahydro-2,3-bispyrrolo[3,2,1-hi]indole, which was reduced with NaCNBH3, converted to the BOC deriv., brominated, and coupled with 4-chlorophenylboronic acid and deprotected to give the 2-(2-chlorophenyl)octahydro-2,3-bispyrrolo[3,2,1-hi]indole II. The invention is also concerned with pharmaceutical formulations comprising these novel compds. as active ingredients and the use of the novel compds. and their formulations in the treatment of certain disorders (no data). The compds. of this invention are serotonin agonists and antagonists and are useful in the control or prevention of central nervous system disorders including obesity, anxiety, depression, psychosis, schizophrenia, sleep disorders, sexual disorders, migraines, conditions assoc. with cephalic pain, social phobias, and gastrointestinal disorders such as dysfunction of the gastrointestinal tract motility.  
 IT 199725-38-7  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (preparation of substituted heterocyclo fused y-carbolines as serotonin agents)  
 RN 199725-38-7 CA  
 CN 2H-Pyrido[4,3-b]indole-2-carboxylic acid, 1,3,4,4a,5,9b-hexahydro-, ethyl ester, (4aR,9bS)-rel- (SCI) (CA INDEX NAME)

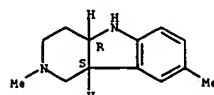
Relative stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

LS ANSWER 13 OF 134 CA COPYRIGHT 2005 ACS ON STN  
 ACCESSION NUMBER: 133:98957 CA  
 TITLE: Extraction and chromatographic separation methods in pharmacokinetic studies of stobadine - an indole-related antioxidant and free-radical scavenger  
 AUTHOR(S): Soltes, L.; Bezak, S.; Ujhazy, E.; Bauer, V.  
 CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, SK-84216, Slovakia  
 SOURCE: Biomedical Chromatography (2000), 14(3), 188-201  
 CODEN: BICHE2; ISSN: 0269-3879  
 PUBLISHER: John Wiley & Sons Ltd.  
 DOCUMENT TYPE: Journal General Review  
 LANGUAGE: English  
 AB A review with over 80 refs. This overview provides comprehensive information on the most relevant results of Stobadine prelin. disposition studies. In order to investigate pharmacokinetic processes of the drug in rats, dogs and in human volunteers, several bioanal. assays based on radiometric, spectrofluorometric, as well as chromatog. determination methods were developed and implemented. In small laboratory animals, the drug absorption, distribution, metabolism and elimination were investigated by administering 3H-labeled Stobadine. Spectrofluorometry was used alternatively for the determination of cold/unlabeled Stobadine in exts. of biomaterials sampled from larger animal species. The chromatog. separation methods proved, however, to be the most advantageous for determining details of the drug disposition and fate in the body.  
 IT 95751-51-2, Stobadine  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (extraction and chromatog. separation methods in pharmacokinetic studies of stobadine)  
 RN 95751-51-2 CA  
 CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, dihydrochloride, (4aR,9bS)- (SCI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



●2 HCl

REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

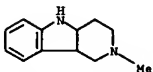
L9 ANSWER 14 OF 134 CA COPYRIGHT 2005 ACS ON STN  
 ACCESSION NUMBER: 133:790 CA  
 TITLE: New use of glutamate antagonists for the treatment of cancer  
 INVENTOR(S): Ikonomidou, Hrisseanthi  
 PATENT ASSIGNEE(S): Germany  
 SOURCE: Eur. Pat. Appl., 21 pp.  
 CODEN: EPKXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1002535	A1	20000524	EP 1998-250380	19981028 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AU 9964750	A1	20000515	AU 1999-64750	19991022 <--
EP 1124553	A1	20010822	EP 1999-952622	19991022 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002528415	T2	20020903	JP 2000-578005	19991022 <--
US 6737692	B1	20040928	US 2001-830354	20010425
US 2005054619	A1	20050310	US 2004-912159	20040806
US 2005054650	A1	20050310	US 2004-912175	20040806
PRIORITY APPLN. INFO.:			EP 1998-250380	A 19981028
			WO 1999-EP8004	V 19991022
			US 2001-830354	A3 20010425

AB New therapies can be devised based upon a demonstration of the role of glutamate in the pathogenesis of cancer. Inhibitors of the interaction of glutamate with the AMPA, kainate, or NMDA receptor complexes are likely to be useful in treating cancer and can be formulated as pharmaceutical comps. They can be identified by appropriate screens.

IT 56223-47-3D, derivs.  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (glutamate antagonists for cancer treatment)

RN 56223-47-3 CA  
 CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2-methyl- (9CI) (CA INDEX NAME)

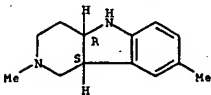


REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 15 OF 134 CA COPYRIGHT 2005 ACS ON STN (Continued)

CRN 85202-17-1  
 CMF C13 H18 N2

Absolute stereochemistry. Rotation (-).



CH 2

CRN 57-10-3  
 CMF C16 H32 O2

HO<sub>2</sub>C-(CH<sub>2</sub>)<sub>14</sub>-Me

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 15 OF 134 CA COPYRIGHT 2005 ACS ON STN  
 ACCESSION NUMBER: 132:273805 CA  
 TITLE: Overview of stobadine bioanalysis: evaluation and application in pharmacokinetics  
 AUTHOR(S): Bauerova, K.  
 CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, 842 16, Slovakia  
 SOURCE: European Journal of Drug Metabolism and Pharmacokinetics (1999), 24(3), 237-242  
 CODEN: EJDPD2 ISSN: 0378-7966  
 PUBLISHER: Medecine et Hygiene  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Besides its many pharmacodynamic actions, the pyridoindole stobadine was found to exert antioxidant activity and thus possesses the potential to protect various tissues against oxidative stress. This overview is focussed on both the evaluation of the chemical procedures used in the bioassay of stobadine and its metabolites and on the comparison of their quality in the light of applicability for preclin. and clin. pharmacokinetic expts. All methods and applications were performed at the Institute of Exptl. Pharmacol., SASc in Bratislava, Slovakia. In pharmacokinetic and toxicokinetic studies, [3H]-labeled stobadine dihydrochloride was administered i.v. or orally to rats in single and repeated doses. Liquid-liquid extraction was used for selective isolation of stobadine and its metabolites from biol. matrix, followed by liquid scintillation quantification. A TLRC method was developed both to check the radiochem. purity of [3H]-stobadine and to quantify the labeled drug in rat plasma. A spectrofluorometric approach was used for determination of stobadine in dog serum and urine after its

administration in the form of either the dihydrochloride or the dipalmitate. The method allowed us to perform a bioavailability study and a long-term toxicol. study. The HPLC method with a limit of detection of 10 ng/mL of plasma proved suitable for calculating the compartmental pharmacokinetic parameters of both salt forms of stobadine administered to dog and man. This method was based on solid-phase extraction procedure by using Separcol SI C18 cartridges. In a GC method, the combination of capillary column separation and nitrogen-specific detection permitted the assay of stobadine concns. as low as 5 ng/mL. The detection limit of the GC/MS method was 1 ng/mL of plasma or of phosphate buffer saline. This method was used for a bioequivalence study of two stobadine dipalmitate dosage forms and for a transdermal penetration study of stobadine acyl derivs. All the developed assays proved to be appropriate for low-concentration determination of stobadine in a wide range of pharmacokinetic studies.

IT 85202-18-2, Stobadine dipalmitate  
 RL: ANT (Analytical); ANST (Analytical study)  
 (stobadine bioanal.: comparative evaluation of various anal. procedures for pharmacokinetic study)

RN 85202-18-2 CA  
 CN Hexadecanoic acid, compd. with (4aR,9bS)-2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-1H-pyrido[4,3-b]indole (2:1) (9CI) (CA INDEX NAME)

CH 1

L9 ANSWER 16 OF 134 CA COPYRIGHT 2005 ACS ON STN

ACCESSION NUMBER: 132:202577 CA  
 TITLE: Bioavailability and pharmacokinetic studies in the development of an oral formulation of stobadine dipalmitate  
 AUTHOR(S): Bauerova, K.; Bohov, P.; Durisova, M.; Bezak, S.  
 CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, Slovakia  
 SOURCE: Methods and Findings in Experimental and Clinical Pharmacology (1999), 21(7), 499-503  
 CODEN: MFEPLX ISSN: 0379-0355  
 PUBLISHER: Frous Science  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The pyridoindole stobadine is a novel drug with antioxidant and cardioprotective properties. The objective of this study was to compare the bioavailability and the main pharmacokinetic parameters of two different stobadine dosage forms, STBtest and STBref, after single oral dosing in the form of gelatine capsules to 6 dogs. The dose ranged from 2.9 to 4.7 mg/kg and a randomized two-period crossover design was applied. To quantify the drug in plasma, a GC/MS method was developed with a quantification limit of 1 ng/mL. The time profiles of stobadine plasma concns. were fitted by pharmacokinetic models. The extent of relative bioavailability ranged between 0.71 and 1.56. Practically no difference was found between the bioavailability rate of the two capsules, expressed as C<sub>max</sub>/AUC, with values ranging from 0.0022-0.0047 min<sup>-1</sup> for STBtest and 0.0022-0.0045 min<sup>-1</sup> for STBref. In conclusion, the technol. difference of the capsules investigated did not yield deviations in either their extent or rate of absorption. Therefore the two stobadine formulations were concluded to be bioequivalent.

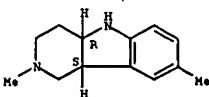
IT 85202-18-2, Stobadine dipalmitate  
 RL: BAC (Biological activity or effector, except adverse); EPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (bioavailability and pharmacokinetic studies in development of oral formulation of stobadine dipalmitate)

RN 85202-18-2 CA  
 CN Hexadecanoic acid, compd. with (4aR,9bS)-2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-1H-pyrido[4,3-b]indole (2:1) (9CI) (CA INDEX NAME)

CH 1

CRN 85202-17-1  
 CMF C13 H18 N2

Absolute stereochemistry. Rotation (-).



CH 2

CRN 57-10-3  
 CMF C16 H32 O2

19 ANSWER 16 OF 134 CA COPYRIGHT 2005 ACS on STN (Continued)

HD<sub>2</sub>C-(CH<sub>2</sub>)<sub>14</sub>-Me

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

19 ANSWER 17 OF 134 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 132:132216 CA

TITLE:

Dopaminergic involvement in the process of reinforcement from diethyl ether vapor in rats  
Pogorelov, Vladimir M.; Kovalev, Georgy I.  
Laboratory of Radioisotopic Researches, Institute of Pharmacology, Russian Academy of Medical Sciences, Moscow, Russia

SOURCE:

Progress in Neuro-Psychopharmacology & Biological Psychiatry (1999), 23(6), 1135-1156  
CODEN: PNPPD7; ISSN: 0278-5846

PUBLISHER:

DOCUMENT TYPE:

LANGUAGE:

AB

1. Male and female Wistar rats were placed in boxes for 30 min daily and allowed to nose-poke in two holes on opposite walls, which opened into evaporation chambers through valves. One chamber contained di-Et ether vapor

another - air, the contents being alternated randomly. Rats inhaled the contents of evaporation chambers while nose-poking differed by the level of intake of di-Et ether vapor. Rats with the intake time of more than 3 s formed about 15% of population. Their preference for di-Et ether was above 0.55. There was significant neg. correlation between the time of vapor inhalation and the time of immobility in forced swimming test in females but not in males. Withdrawal of di-Et ether vapor decreased the inhalation time. On the first day after ether deprivation inhalation time rose above average level. Relationship between concentration of ether vapor and the

time of its inhalation was inverted U-shaped function. Substitution of acetone vapor elevated the time of the vapor inhalation. D-amphetamine in dose 0.05 mg/kg elevated the time of inhalation of and preference for ether vapor in some rats. In doses 0.05-1.0 mg/kg amphetamine selectively suppressed the time of vapor inhalation. Haloperidol in doses 0.05 and 0.1 mg/kg elevated the time of vapor inhalation on the first day in females and suppressed it in doses 0.05-0.3 mg/kg dose-dependently on the second day. Atypical neuroleptic cis-carbidine elevated the time of vapor inhalation in doses 2.5 and 5.0 mg/kg and suppressed it at 10 mg/kg. Di-Et ether vapor can be established as reinforcer in rats. Female rats are more liable to reinforcement from ether vapor than males and show more pronounced response to haloperidol. This may be related to its more active behavior in the forced swimming situation. The results point to potential involvement of dopamine system in the process of reinforcement from ether vapor.

IT 94452-31-0, cis-Carbidine

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

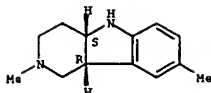
RN

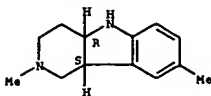
CN

94452-31-0 CA  
1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, dihydrochloride, (4aR,9bS)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

19 ANSWER 17 OF 134 CA COPYRIGHT 2005 ACS on STN (Continued)

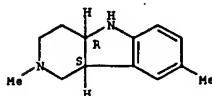




REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ACCESSION NUMBER: 132:73508 CA  
 TITLE: Evaluation of long-term administration of the antioxidant stobadine on exploratory behavior in rats of both genders  
 AUTHOR(S): Dubovický, M.; Ujhazy, E.; Kováčovský, P.; Rychlík, I.; Janský, J.  
 CORPORATE SOURCE: Institute of Experimental Pharmacology SAS, Bratislava, 842 16, Slovakia  
 SOURCE: Journal of Applied Toxicology (1998), 19(6), 431-436  
 CODEN: JJATDK ISSN: 0260-437X  
 PUBLISHER: John Wiley & Sons Ltd.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Stobadine (STO) is a prospective neuro- and cardioprotective drug with high antioxidative properties. The aim of this study was to ascertain the effect of long-term administration of STO on exploratory behavior and habituation processes in adult virgin female and male rats. Stobadine was administered by oral gavage in a single dose of 50 mg kg<sup>-1</sup> day<sup>-1</sup> for a total of 56 days. The animals were tested for exploratory behavior-intensity of motor and vertical activity in an open field test in three blocks of measurements (initial screening; after 56 days of STO administration; and 28 days after the last treatment). The rate of decline of motor activity was evaluated during four consecutive days of testing (interrupted habituation). Administration of STO resulted in transient inhibition of exploratory behavior in female rats without overtly detectable toxicity. Exploratory behavior of males was not affected by STO treatment.  
 IT 95751-51-2, Stobadine  
 RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (evaluation of long-term administration of the antioxidant stobadine on exploratory behavior in rats of both genders)  
 RN 95751-51-2 CA  
 CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, dihydrochloride, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

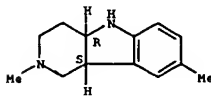


● 2 HCl

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ACCESSION NUMBER: 132:18356 CA  
 TITLE: Pharmacokinetic study of stobadine  
 AUTHOR(S): Bezek, S.; Soltes, L.; Scannar, V.; Bauerova, K.; Kalley, Z.; Durisova, M.; Mihalova, D.; Bohov, P.; Faberova, V.; Kukan, M.; Trnovec, T.; Koprda, V.  
 CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, 84216, Slovakia  
 SOURCE: Life Sciences (1998), 65(18/19), 2003-2005  
 CODEN: LIFSAR ISSN: 0024-3205  
 PUBLISHER: Elsevier Science Inc.  
 DOCUMENT TYPE: Journal; General Review  
 LANGUAGE: English  
 AB A review with 16 refs. The most important results of stobadine pharmacokinetic studies in rats, dogs, and humans are presented. Stobadine dihydrochloride and stobadine dipalmitate were used for i.v. and oral administration, resp. TLC, HPLC, GLC, GC-MS, radiometric, and fluorometric methods were developed for the studies of stobadine and its metabolites.  
 IT 85202-18-2  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (stobadine pharmacokinetics in rats, dogs and humans)  
 RN 85202-18-2 CA  
 CN Hexadecanoic acid, compd. with (4aR,9bS)-2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-1H-pyrido[4,3-b]indole (2:1) (9CI) (CA INDEX NAME)  
 CM 1  
 CRN 85202-17-1  
 CMF C13 H18 N2

Absolute stereochemistry. Rotation (-).



CM 2

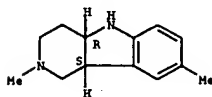
CRN 57-10-3  
 CMF C16 H32 O2

HO<sub>2</sub>C-(CH<sub>2</sub>)<sub>14</sub>-Me

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ACCESSION NUMBER: 132:8961 CA  
 TITLE: Membrane ion transport systems during oxidative stress in rodent brain: protective effect of stobadine and other antioxidants  
 AUTHOR(S): Lehotsky, J.; Kaplan, P.; Racsay, P.; Matejovicova, M.; Drgova, A.; Mezesova, V.  
 CORPORATE SOURCE: Jassienius Medical Faculty, Comenius University, Martin, SK-03601, Slovakia  
 SOURCE: Life Sciences (1999), 65(18/19), 1951-1958  
 CODEN: LIFSAR ISSN: 0024-3205  
 PUBLISHER: Elsevier Science Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The effect of oxidative stress in vitro induced by radical generating systems (RGS) (Fe<sup>2+</sup>-EDTA and Fe<sup>2+</sup>-EDTA plus H<sub>2</sub>O<sub>2</sub>) on synaptosomal and microsomal ion transport systems as well as on the membrane fluidity was investigated. Oxidative insult reduced Na<sup>+</sup>/K<sup>+</sup>-ATPase activity by 50.7% and Na<sup>+</sup>-dependent Ca<sup>2+</sup> uptake measured in choline media by 46.7%. Membrane fluidity was also significantly reduced as observed with the fluorescent probe. Stobadine (ST) prevented the decrease in membrane fluidity and Na<sup>+</sup>-dependent Ca<sup>2+</sup> uptake, however Na<sup>+</sup>/K<sup>+</sup>-ATPase activity was only partially protected, indicating a more complex mechanism of inhibition. Incubation of microsomes with RGS led to the loss of ability of membranes to sequester Ca<sup>2+</sup>, as well as to the decrease of Ca<sup>2+</sup>-ATPase activity and to the increase of Ca<sup>2+</sup> permeability to 125.4%. The relative potency of the two RGS to decrease membrane fluidity correlated well with the system's potencies to induce lipid peroxidation. The extent of protection against depression of Ca<sup>2+</sup> uptake values and Ca<sup>2+</sup>-ATPase activity by membrane soluble antioxidants (U-74500A, U-83836B, t-butylated hydroxytoluene-BHT and ST) was dependent on the exptl. conditions and on the dose and nature of antioxidant used. ST seems to be at least as effective as BHT and 21-aminosteroids, and more potent than tocopherol acetate. Water soluble glutathione had no significant effect on the RGS induced inhibition of Ca<sup>2+</sup>-ATPase activity. Combination of ST with glutathione enhanced ST antioxidant efficacy, so drug combination might be beneficial therapeutically.  
 IT 95751-51-2, Stobadine  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (protective effect of stobadine and other antioxidants on membrane ion transport systems during oxidative stress in rodent brain)  
 RN 95751-51-2 CA  
 CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, dihydrochloride, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● 2 HCl

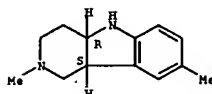
19 ANSWER 21 OF 134 CA COPYRIGHT 2005 ACS on STN (Continued)

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

19 ANSWER 22 OF 134 CA COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 132:8959 CA  
 TITLE: EPR spectroscopy of free radical intermediates of antiarrhythmic-antihypoxic drug stobadine, a pyridoindole derivative  
 AUTHOR(S): Misik, Vladimir; Ondrias, Karol; Stasko, Andrej  
 CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, 84216, Slovakia  
 SOURCE: Life Sciences (1999), 65(18/19), 1879-1881  
 CODEN: LIFSAK; ISSN: 0024-3205  
 PUBLISHER: Elsevier Science Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Mechanisms of antioxidant action of stobadine, a pyridoindole derivative with cardioprotective and antihypoxic properties, has been probed using EPR spectroscopy. Oxidation of stobadine by PbO<sub>2</sub>/LbOOH in benzene results in the formation of nitroxide radical observable directly by EPR spectroscopy at room temperature, indicating conversion of indolic amino group to the corresponding nitroxide.  
 IT 95751-51-2, Stobadine  
 RL: RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)  
 (EPR of free radical intermediates of antiarrhythmic-antihypoxic drug stobadine)  
 RN 95751-51-2 CA  
 CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, dihydrochloride, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● 2 HCl

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

19 ANSWER 23 OF 134 CA COPYRIGHT 2005 ACS on STN

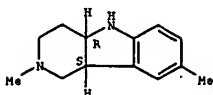
ACCESSION NUMBER: 132:8957 CA  
 TITLE: Stobadine: bellwether of a broader view of drug actions  
 AUTHOR(S): Vincenzi, Frank F.; Hinds, Thomas R.  
 CORPORATE SOURCE: Department of Pharmacology, University of Washington, Seattle, WA, 98195-7280, USA  
 SOURCE: Life Sciences (1999), 65(18/19), 1857-1864  
 CODEN: LIFSAK; ISSN: 0024-3205  
 PUBLISHER: Elsevier Science Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Stobadine was recognized early in its development as having antioxidant properties. A number of labs. found assocns. between the antioxidant properties of stobadine and its potential beneficial effects. We found that stobadine acted as an antioxidant in a modification of an oxygen radical absorbance capacity assay. Similar results were observed with other drugs, including tirilazad and pramipexole. We suggest that stobadine and certain other drugs exhibit antioxidant properties in both hydrophilic and hydrophobic environments. Other drugs have been developed for their antioxidant properties and some currently marketed drugs have antioxidant properties. Although they may not have been explicitly sought during development, at least some of the beneficial effects may be related to antioxidant properties and/or scavenging of free radicals. Because stobadine was one of the first drugs for which useful properties were associated with its antioxidant actions, stobadine may be seen as a bellwether of a broader view of pharmacol. actions - a view that encompasses antioxidant properties as a useful basis of therapeutic effects.

IT 85202-17-1, Stobadine  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (stobadine: bellwether of a broader view of antioxidant drug actions)

RN 85202-17-1 CA  
 CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

19 ANSWER 24 OF 134 CA COPYRIGHT 2005 ACS on STN

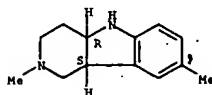
ACCESSION NUMBER: 132:8879 CA  
 TITLE: Oxidative modification of serum albumin in an experimental glycation model of diabetes mellitus in vitro: effect of the pyridoindole antioxidant stobadine  
 AUTHOR(S): Stefek, M.; Krizanova, L.; Trnkova, Z.  
 CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, 842 16, Slovakia  
 SOURCE: Life Sciences (1999), 65(18/19), 1995-1997  
 CODEN: LIFSAK; ISSN: 0024-3205  
 PUBLISHER: Elsevier Science Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Under conditions of an exptl. in vitro glycation model, the pyridoindole antioxidant stobadine significantly inhibited glycation-related fluorescence changes of bovine serum albumin as well as the yield of 2,4-dinitrophenyl-hydrazine-reactive carbonyls with an efficacy comparable to that of the reference antioxidants Trolox C and 2-keto-4-methylbutyric acid, and more efficiently than did aminoguanidine. Since stobadine did not affect the covalent binding of glucose, the protective effect may be explained by the ability of the drug to eliminate free radical intermediates of glyco-oxidation reactions, operative after the preceding glycation steps.

IT 85202-17-1, Stobadine  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (pyridoindole antioxidant stobadine effect on oxidative modification of serum albumin in glycation model of diabetes mellitus)

RN 85202-17-1 CA  
 CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

19 ANSWER 25 OF 134 CA COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 132:8624 CA  
 TITLE: Indole derivatives as neuroprotectants  
 AUTHOR(S): Solc, Svorad  
 CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, SK-842 16, Slovakia  
 SOURCE: Life Sciences (1999), 65(18/19), 1943-1950  
 CODEN: LIFSAK ISSN: 0024-3205  
 PUBLISHER: Elsevier Science Inc.  
 DOCUMENT TYPE: Journal General Review  
 LANGUAGE: English

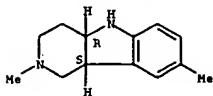
AB A review with 69 refs. It seems to be satisfactorily proved that reactive oxygen species (ROS) participate in numerous pathol. processes in the nervous system (NS). Compds. able to interfere with the action of ROS might be useful in prevention and treatment of these pathologies. The search is focused on compds. with a suitable spectrum of pharmacol. and pharmacokinetic properties, among which indole derivs. are distinct group with great potential to be further developed. The paper presents an overview of indole derived compds. in which protective action has been demonstrated in the NS in situations in which ROS are excessively generated, such as chemical induced oxidative stress, hypoxia/reoxygenation, ischemia/reperfusion. These compds. include indoleamines (melatonin), carbazoles (carvedilol), carbolines (tetrahydrocarbolines, pyrimidoindoles, vinpocetine). Special attention is paid to the  $\gamma$ -carboline stobadine. A range of effects which seem to be associated with its neuroprotective actions (antioxidant and ROS scavenging effects, capability to pass the hematoencephalic barrier, pharmacokinetic properties, etc.) are considered. A novel compound with pyrimidoindole structure (U-101033E) is mentioned. Attention is drawn also to the neurotoxic potential demonstrated in some carbolines (2-amino- $\alpha$ -carbolines, halogenated tetrahydro- $\beta$ -carbolines "TaClo", harmaline, norharmaline). The indole nucleus seems to be a promising basis for design and synthesis of new derivs. able to protect the NS against oxidative stress in a variety of acute and chronic NS pathologies.

IT 95751-51-2, Stobadine  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(Indole derivs. as neuroprotectants)

RN 95751-51-2 CA  
 CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, dihydrochloride, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● 2 HCl

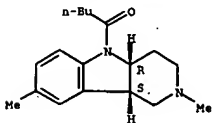
19 ANSWER 26 OF 134 CA COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 132:3153 CA  
 TITLE: Kinetics of hydrolysis of acetyl, valeroyl and nicotinoyl acyl derivatives of stobadine  
 AUTHOR(S): Stankovicova, M.; Bezakova, Z.; Benes, L.  
 CORPORATE SOURCE: Department of Pharmaceutical Chemistry, Faculty of Pharmacy of Comenius University, Bratislava, 832 32, Slovakia  
 SOURCE: Life Sciences (1999), 65(18/19), 2007-2010  
 CODEN: LIFSAK ISSN: 0024-3205  
 PUBLISHER: Elsevier Science Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The present work deals with the kinetics of hydrolysis of the acyl derivs. of stobadine, an originally synthesized potential antiarrhythmic and antihypoxic drug, which was found to have also an excellent scavenging effect on reactive oxygen species. The acyl derivs. of stobadine, which possess high lipophilicity, represent model blood-brain barrier penetrating agents. It is assumed that the acyl derivs. of stobadine may act as prodrugs which are hydrolyzed in different biol. tissues to release the active drug. The decomposition of three acyl derivs. of stobadine was studied in acidic, basic and neutral buffer solns. at constant ionic strength (0.1 mol/L) at 25° and 70°C using UV spectrophotometric method. The pseudo first-order rate consts. and the pH-rate profile for the degradation of acetyl, valeroyl, and nicotinoyl derivs. of stobadine were determined. Confirmation that stobadine was the first degradation product was provided by thin-layer chromatog.

IT 201608-29-9  
 RL: PEP (Physical, engineering or chemical process); PRP (Properties); RCT (Reactant); PROC (Process); RACT (Reactant or reagent)  
 (Kinetics and mechanism of hydrolysis of acetyl, valeroyl, and nicotinoyl acyl derivs. of stobadine)

RN 201608-29-9 CA  
 CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-5-(1-oxopentyl)-, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

19 ANSWER 25 OF 134 CA COPYRIGHT 2005 ACS on STN (Continued)  
 REFERENCE COUNT: 75 THERE ARE 75 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

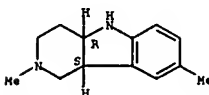
19 ANSWER 27 OF 134 CA COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 131:349826 CA  
 TITLE: Reactive oxygen species induced smooth muscle responses in the intestine, airways and vessels and the effect of antioxidants  
 AUTHOR(S): Bauer, V.; Sotnikova, R.; Machova, J.; Matyas, S.; Pucovsky, V.; Stefek, M.  
 CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, 842 16, Slovakia  
 SOURCE: Life Sciences (1999), 65(18/19), 1909-1917  
 CODEN: LIFSAK ISSN: 0024-3205  
 PUBLISHER: Elsevier Science Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Numerous exptl. data confirm the importance of reactive oxygen species (ROS) in physiol. activities of smooth muscles and in the pathogenesis of various diseases with altered function of smooth muscles. The present study shows that smooth muscles of the intestine, airways and vessels, as well as their epithelium, endothelium and innervations, might be important targets of the ROS action. We demonstrated differences among the actions of various ROS (endogenous, exogenous, produced enzymically, non-enzymically) as well as among their actions in different smooth muscle tissues. Our results indicate that ROS are involved in changes in muscle tone, membrane conductance, calcium homeostasis, calcium-dependent processes, as well as in eicosanoid and nitric oxide metabolism. The effects of antioxidative enzymes (superoxide dismutase, catalase), of several drugs of natural origin (e.g. Kambo Medicines) and synthetic agents (e.g. stobadine, nitroglycerine, ACE inhibitors) suggest that smooth muscle tissues are useful models to study ROS action and drug intervention in ROS induced injuries.

IT 85202-17-1, Stobadine  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (Intestine, blood vessels and airway smooth muscle responses to reactive oxygen species and effect of antioxidants)

RN 85202-17-1 CA  
 CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 28 OF 134 CA COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 131:346326 CA  
 TITLE: Protective effect of stobadine in experimental colitis  
 AUTHOR(S): Nosál, Viera; Bauer, Viktor  
 CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, 84216, Slovakia  
 SOURCE: Life Sciences (1999), 65(18/19), 1919-1921  
 CODEN: LIFSAK ISSN: 0024-3205  
 PUBLISHER: Elsevier Science Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB To assess the role of reactive oxygen species in inflammatory bowel disease, the effects of the antioxidant and free radical scavenger drug stobadine were studied in acetic acid-induced exptl. colitis in male Wistar rats. Stobadine given locally into the colon decreased the colonic mucosal injury, abolished the increase in myeloperoxidase activity, attenuated the enhanced vascular permeability, and prevented the depletion of reduced glutathione. The decrease in free radical production

and oxidative damage in the inflamed colonic mucosa may be used as a complementary treatment in ulcerative colitis.

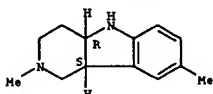
IT 85202-17-1, Stobadine  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(stobadine protective effects in exptl. colitis in rats)

RN 85202-17-1 CA

CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 29 OF 134 CA COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 131:346287 CA  
 TITLE: Placental transfer of stobadine in rabbits  
 AUTHOR(S): Ujhazy, E.; Dubovický, M.; Soltes, L.; Faberova, V.; Zemanek, M.; Gajdosik, A.  
 CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, Slovakia  
 SOURCE: Life Sciences (1999), 65(18/19), 2011-2014  
 CODEN: LIFSAK ISSN: 0024-3205  
 PUBLISHER: Elsevier Science Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Stobadine, a pyridoindole antioxidant, was investigated for its placental transfer and distribution in New Zealand white rabbits on the 27th day of gestation. The concns. of stobadine were determined in maternal and fetal organs (plasma, brain, heart) at 30, 60, 120, and 360 min after oral administration of the drug in a dose of 5 mg/kg. The results obtained proved that after oral stobadine intake by rabbits at the stage of advanced pregnancy both maternal and fetal organs were under a certain drug level which could act protectively against oxidative stress - frequently occurring during late organogenesis, fetal stages and delivery, as well as during early postnatal development.

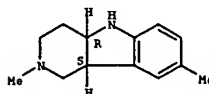
IT 85202-17-1, Stobadine  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(placental transfer of stobadine)

RN 85202-17-1 CA

CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 30 OF 134 CA COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 131:346285 CA  
 TITLE: Aggregation of human blood platelets in the presence of the pyridoindole stobadine  
 AUTHOR(S): Jancinova, Viera; Nosál, Rado; Danhelova, Edita  
 CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, 84216, Slovakia  
 SOURCE: Life Sciences (1999), 65(18/19), 1983-1986  
 CODEN: LIFSAK ISSN: 0024-3205  
 PUBLISHER: Elsevier Science Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The effects of stobadine dihydrochloride, an antiarrhythmic and cardioprotective drug with antioxidant and neuroprotective properties, were studied in assays of human blood platelet in vitro aggregation. Pretreatment of platelets with stobadine for 30 s inhibited the stimulated platelet aggregation in a dose-dependent way. Depending on the aggregation stimulus used, the minimal effective concns. of the drug were 1 µM (adrenaline), 200 µM (ADP), and 1000 µM (PMA). Aggregation induced with thrombin or the Ca2+-ionophore A-23187 was not changed in the presence of stobadine even at 1000 µM. Addition of stobadine 30 s after adrenaline was also effective and terminated the aggregation (100 and 1000 µM) or delayed the onset of its second phase (10 µM). Thus, stobadine is a potent inhibitor of adrenaline-induced blood platelet aggregation, indicating an involvement in the antithrombotic and cytoprotective activities.

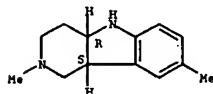
IT 95751-51-2, Stobadine dihydrochloride  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(stobadine inhibition of human blood platelet aggregation in vitro)

RN 95751-51-2 CA

CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, dihydrochloride, (4aR,9bS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● 2 HCl

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 31 OF 134 CA COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 131:346280 CA  
 TITLE: Effect of stobadine on cardiac injury induced by ischemia and reperfusion  
 AUTHOR(S): Knezl, V.; Sotnikova, R.; Okruhlicova, L.; Navarova, J.  
 CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, 84216, Slovakia  
 SOURCE: Life Sciences (1999), 65(18/19), 1931-1933  
 CODEN: LIFSAK ISSN: 0024-3205  
 PUBLISHER: Elsevier Science Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The effects of the antioxidant drug stobadine on ischemia/reperfusion injury were studied in the isolated Langendorff rat heart preps. Ischemia was induced by 30-min stop-flow and the reperfusion lasted 30 min. Reperfusion of the ischemic heart induced dysrhythmias, with the most severe ones occurring in the first minutes of reperfusion. An increase in coronary perfusion pressure was observed after 15 min of reperfusion. Stobadine (10-6 M applied 3 min before the onset of ischemia and during reperfusion) prevented the deleterious effects to develop fully. The protective effects of stobadine seem to be due to its antioxidant properties.

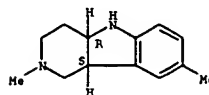
IT 85202-17-1, Stobadine  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(stobadine protective effects in ischemia and reperfusion injury in isolated rat hearts)

RN 85202-17-1 CA

CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

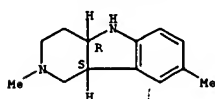
L9 ANSWER 32 OF 134 CA COPYRIGHT 2005 ACS ON STN  
 ACCESSION NUMBER: 131:346279 CA  
 TITLE: Stobadine inhibits lysosomal enzyme release in vivo and in vitro  
 AUTHOR(S): Navarova, Jana; Macickova, Tatiana; Horakova, Katarina; Urbancikova, Miroslava  
 CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, 84216, Slovakia  
 SOURCE: Life Sciences (1999), 65(18/19), 1905-1907  
 CODEN: LIFSAK ISSN: 0024-3205  
 PUBLISHER: Elsevier Science Inc.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The ability of stobadine dihydrochloride, a cardioprotective drug with antiarrhythmic, antihypoxic and oxygen free radical scavenging properties, to protect cells against cyclophosphamide-induced toxic and cytotoxic damage was studied in vivo and in vitro. The cyclophosphamide toxic damage in female ICR mice was accompanied by marked increase in the activity of lysosomal enzymes (acid phosphatase, N-acetyl-β-D-glucosaminidase) in the spleen and kidney. Administration of stobadine prior to cyclophosphamide inhibited these biochem. changes. The in vivo protective effects of stobadine were comparable with the in vitro effects in HeLa cells.

IT 95751-51-2, Stobadine  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
 (stobadine inhibits lysosomal enzyme release from mouse spleen and kidney and from HeLa cells in vitro)

RN 95751-51-2 CA  
 CN 1H-Pyrido(4,3-b)indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, dihydrochloride, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● 2 HCl

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 34 OF 134 CA COPYRIGHT 2005 ACS ON STN  
 ACCESSION NUMBER: 130:162954 CA  
 TITLE: Endothelial protective effect of stobadine on ischemia/reperfusion-induced injury  
 AUTHOR(S): Sotnikova, R.; Okruhlicova, L.; Noskovic, P.  
 CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, Slovakia  
 SOURCE: General Physiology and Biophysics (1998), 17(3), 253-264  
 CODEN: GPBIE2 ISSN: 0231-5882  
 PUBLISHER: Institute of Molecular Physiology and Genetics, Slovak Academy of Sciences  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The aim of the present study was to evaluate the influence of the antioxidant stobadine on changes in the reactivity of the rat abdominal aorta induced by ischemia and reperfusion (I/R). In anesthetized male rats, in vivo ischemia was elicited by occlusion of the abdominal aorta for 18 h; reperfusion lasted 30 min. The aortal rings were taken from the reperfusion portion. Decreased relaxant response to acetylcholine, as a consequence of endothelial injury, was seen after I/R. We also demonstrated I/R-induced reversible ultrastructural changes both in endothelial and smooth muscle cells, predominantly in the mitochondria. Lipid peroxidn. was increased in homogenates of I/R aortae; the concentration of

thiobarbituric acid reactive substances (TBARS) increased from a control value of  $0.97 \pm 0.03$  to  $2.57 \pm 0.06$  nmol/1/mg protein. Stobadine (2 mg/kg i.v., 5 min before starting reperfusion) protected the abdominal aorta against I/R-induced decrease of acetylcholine relaxation, and prevented changes in mitochondria and an increase of TBARS concentration

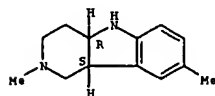
The protective effect of stobadine seems to be due to its antioxidant properties.

IT 85202-17-1, Stobadine  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(endothelial protective effect of stobadine on ischemia/reperfusion-induced injury)

RN 85202-17-1 CA  
 CN 1H-Pyrido(4,3-b)indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 33 OF 134 CA COPYRIGHT 2005 ACS ON STN  
 ACCESSION NUMBER: 131:345989 CA  
 TITLE: Antimutagenic effects of stobadine: review of results  
 AUTHOR(S): Chorvatovicova, Darina; Horvathova, Eva; Slamenova, Darina  
 CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, Slovakia  
 SOURCE: Life Sciences (1999), 65(18/19), 2015-2017  
 CODEN: LIFSAK ISSN: 0024-3205  
 PUBLISHER: Elsevier Science Inc.  
 DOCUMENT TYPE: Journal; General Review  
 LANGUAGE: English

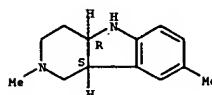
AB A review and discussion with 14 refs. which summarizes the results of previously published studies testifying the hypothesis of the antimutagenic effect of stobadine (STB) in vivo and in vitro. The micronucleus test was used in in vivo expts. with ICR mice. Oral pretreatment with STB significantly decreased the mutagenic effect of cyclophosphamide (CP) in a concentration-dependent way. The protective effect of

STB was confirmed in fetuses of CP-treated mice. STB pretreatment exerted also a radioprotective effect in Co60-irradiated mice. The ineffectiveness of STB posttreatment is indicative of its effect operative in the initiation of mutagenesis and of its radical-scavenging mechanism. The ability of STB to reduce N-methyl-N'-nitro-N-nitrosoguanidine (MNNG)-induced gene mutations and MNNG-induced calcosin/Ryanod's phenomenon/esophageal dysmotility/sclerodactyl/teleangiectasia variant of scleroderma(CREST)-pos. and CREST-neg. micronuclei in V-79 cells was tested in in vitro expts. It was found that this drug reduced the level of both gene mutations and CREST-neg. micronuclei mainly if given as pretreatment before exposure of cells to MNNG. Thus, STB may have inhibited mutagenesis not only by scavenging reactive oxygen species, but also as a result of the induction of metabolic enzymes, which reduced the level of DNA lesions.

IT 85202-17-1, Stobadine  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (antimutagenic effects of stobadine)

RN 85202-17-1 CA  
 CN 1H-Pyrido(4,3-b)indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 35 OF 134 CA COPYRIGHT 2005 ACS ON STN  
 ACCESSION NUMBER: 130:60575 CA  
 TITLE: Studies of the kinetics of hydrolysis of acyl derivatives of stobadine, the prodrug forms of oxygen free radical scavengers. Part 1: acid hydrolysis  
 AUTHOR(S): Stankovicova, M.; Bezakova, Z.; Benas, L.  
 CORPORATE SOURCE: Katedra farmaceutickej chemie Farmaceutickej fakulty, Univerzity Komenského, Bratislava, Slovakia  
 SOURCE: Ceska a Slovenska Farmacie (1998), 47(5), 239-242  
 CODEN: CSLFEK ISSN: 1210-7816  
 PUBLISHER: Ceska Lekarska Spolecnost J. Ev. Purkyne  
 DOCUMENT TYPE: Journal  
 LANGUAGE: Slovak

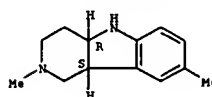
AB Stobadine, (-)-cis-2,8-dimethyl-2,3,4,4a,5,9a-hexahydro-1H-pyrido(4,3b)-indole, is a substance with potential antiarrhythmic and antihypoxic effects, in which also a marked radical-scavenging effect has been found. Stobadine acyl derivs. were prepared and it is assumed that the active principle will be released from them by hydrolyzing in various biol. tissues. The present paper examines the kinetics of acid hydrolysis of 13 stobadine derivs. Decomposition of substances was studied in the medium of hydrochloric acid 0.1 mL.l-1 at 20 and 70 °C spectrophotometrically in the UV region and rate consts. of hydrolysis were determined. The methods of

thin-layer and gas chromatog. confirmed that stobadine is released from the prodrug form.

IT 85202-17-1D, Stobadine, acyl derivs.  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (kinetics of hydrolysis of acyl derivs. of stobadine, the prodrug forms of oxygen free radical scavengers)

RN 85202-17-1 CA  
 CN 1H-Pyrido(4,3-b)indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).





19 ANSWER 36 OF 134 CA COPYRIGHT 2005 ACS ON STN

ACCESSION NUMBER: 129:23 CA

TITLE: Antioxidant and pharmacodynamic effects of pyridindole stobadine

AUTHOR(S): Horakova, B.; Stolic, S.

CORPORATE SOURCE: Institute Experimental Pharmacology, Slovak Academy Sciences, Bratislava, SK-842 16, Slovakia

SOURCE: General Pharmacology (1998), 30(5), 627-638

CODEN: GRPHDP; ISSN: 0306-3623

PUBLISHER: Elsevier Science Inc.

DOCUMENT TYPE: Journal: General Review

LANGUAGE: English

AB A review with many refs. 1. The review summarizes the most important data known so far on chemical, pharmacodynamics, toxicol. and clinics of the investigational agent, pyridindole stobadine. 2. Stobadine was shown to be able to scavenge hydroxyl, peroxyl and alkoxyl radicals, to quench singlet oxygen, to repair oxidized amino acids and to preserve oxidation of SH groups by one-electron donation. These effects originated from its ability to form a stable nitrogen-centered radical on indole nitrogen. Consequently, it was able to diminish lipid peroxidation and protein impairment under oxidative stress. 3. In various in vitro and in vivo animal models, stobadine was shown to diminish the impairment of the myocardium induced by mechanisms involving reactive oxygen species (e.g., myocardial infarction, hypoxia/reoxygenation, catecholamine overexposure). 4. The neuroprotective effect of stobadine was demonstrated in a series of in vivo and in vitro models (brain in situ, brain slices, spinal cord, autonomic ganglia, etc.) during ischemia/reperfusion and hypoxia/reoxygenation or in the presence of chemical systems generating free oxygen radicals, and so forth. Stobadine improved animal survival rate and synaptic transmission recovery, maintained SH tissue level and diminished lipid peroxidation, as well as impairment of Ca-sequestering intracellular systems. 5. Oxidation of low-density lipoproteins (LDLs), which plays a major role in the development of atherosclerosis, was decreased by stobadine in vitro. Both lipid and protein (apo B) components of LDL were protected against Cu<sup>2+</sup>-induced oxidation by this agent. 6. Stobadine proved to be an effective protectant in models of free radical pathology. In vivo, such as cyclophosphamide-, MNNG- or 60Co-induced mutagenesis and alloxan-induced hyperglycemia. 7. Besides other remarkable pharmacodynamic effects, stobadine exerts antidiarrhythmic, local anesthetic,  $\alpha$ -adrenolytic, antihistaminic, myorelaxant and antitumorogenic actions. 8. Pharmacokinetic analyses demonstrated that stobadine was readily absorbed from the gastrointestinal tract. Thanks to its balanced lipo-hydrophilic properties, it was distributed over both water and lipid phases in biol. tissues. It was shown to easily penetrate the blood-brain barrier. 9. Acute, subchronic and chronic toxicity studies in several animal species, as well as numerous analyses of embryotoxicity, teratogenicity, mutagenicity and genotoxicity, revealed only a negligible toxic potential of this agent. 10. Phase-one clin. study demonstrated safety of the compound. Only slight side effects—namely, a slight hypotension and a slight sedative effect—were observed subsequent to the highest dose used. In phase-two clin.

study, the patients with angina pectoris treated for 4 wk with stobadine showed a significant decrease in the frequency of anginal attacks, in the number of self-administrations of sublingual nitroglycerin and in plasma lipoprotein, cholesterol and triglyceride levels. A slight decrease in systolic and diastolic blood pressure also was observed. 11. It is suggested

19 ANSWER 36 OF 134 CA COPYRIGHT 2005 ACS ON STN (Continued)

that stobadine may be considered a contribution to the search for new effective cardio- and neuroprotectants based on antioxidant or free radical scavenging mechanisms of action.

IT 85202-18-2, DP 1031

RI: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (antioxidant and pharmacodynamic effects of pyridindole stobadine)

RN 85202-18-2 CA

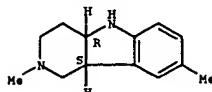
CN Hexadecanoic acid, compd. with (4aR,9bS)-2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-1H-pyrido[4,3-b]indole (2:1) (9CI) (CA INDEX NAME)

CM 1

CRN 85202-17-1

CMF C13 H18 N2

Absolute stereochemistry. Rotation (-).



CM 2

CRN 57-10-3

CMF C16 H32 O2

HO<sub>2</sub>C-(CH<sub>2</sub>)<sub>14</sub>-Me

REFERENCE COUNT: 139 THERE ARE 139 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

19 ANSWER 37 OF 134 CA COPYRIGHT 2005 ACS ON STN

ACCESSION NUMBER: 129:238901 CA

TITLE: Ion-pair extraction of [3H]stobadine from biological fluids

AUTHOR(S): Scasnar, V.

CORPORATE SOURCE: Institute Experimental Pharmacology, Slovak Academy Sciences, Bratislava, 84216, Slovakia

SOURCE: Journal of Radioanalytical and Nuclear Chemistry (1998), 228(1-2), 99-104

CODEN: JRNCHM; ISSN: 0236-5731

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A simple and specific radiometric assay was developed for the determination of

stobadine, a cardioprotective drug, in blood serum of exptl. animals. The assay is based on a single extraction step of the radioactively

labeled drug from serum into the benzene solution of dicarbolide of cobalt followed by quantitation of the extracted radioactivity by liquid scintillation counting. The extraction mechanism involves the ion-pair formation between the protonated mol. of stobadine and the hydrophobic, neg. charged mol. of dicarbolide of cobalt. The extraction yield of stobadine

from 1 mL of serum was 95% in the concentration range from 1 to 6000 ng/mL.

The co-extraction of metabolites was <5%. The method was applied to the determination of stobadine in serum of dogs and the data obtained were in a good agreement with those obtained by high performance liquid chromatog.

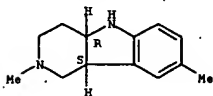
IT 95751-51-2, Stobadine dihydrochloride

RI: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (ion-pair extraction of [3H]stobadine from biol. fluids)

RN 95751-51-2 CA

CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, dihydrochloride, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● 2 HCl

19 ANSWER 38 OF 134 CA COPYRIGHT 2005 ACS ON STN

ACCESSION NUMBER: 128:123776 CA

TITLE: High-molecular-weight hyaluronan - a valuable tool in testing the antioxidative activity of amphiphilic drugs stobadine and vinpocetine

AUTHOR(S): Orvisky, E.; Soltes, L.; Stancikova, Maria

CORPORATE SOURCE: Research Institute of Rheumatic Diseases, Piest'any, SK-92101, Slovakia

SOURCE: Journal of Pharmaceutical and Biomedical Analysis (1997), 16(3), 419-424

CODEN: JPBADA; ISSN: 0731-7095

PUBLISHER: Elsevier Science B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The antioxidative activity of stobadine and vinpocetine was studied in vitro by measuring their inhibition effect on the depolym. of the high-mol.-weight hyaluronan by hydroxyl radicals. The radicals were generated by the Cu<sup>2+</sup> - H<sub>2</sub>O<sub>2</sub> system. Hyaluronan depolym. was monitored by size exclusion chromatog. The antioxidative activity of stobadine and vinpocetine was compared to that of D-mannitol. A 50% inhibition of hyaluronan depolym. was reached at stobadine and vinpocetine concns. of 1.7·10<sup>-6</sup> and 3.0·10<sup>-7</sup> mol l<sup>-1</sup>, resp., while a D-mannitol level of 2.6·10<sup>-3</sup> mol l<sup>-1</sup> was needed to achieve the same inhibitory effect.

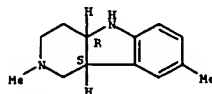
IT 85202-17-1, Stobadine

RI: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BPR (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (high-mol.-weight hyaluronan in testing of antioxidative activity of amphiphilic drugs stobadine and vinpocetine)

RN 85202-17-1 CA

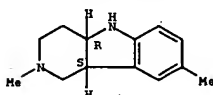
CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 39 OF 134 CA COPYRIGHT 2005 ACS ON STN  
 ACCESSION NUMBER: 128:112503 CA  
 TITLE: Effective one/two step purification of various materials by solid-phase extraction  
 AUTHOR(S): Soltes, Ladislav; Schille, Bernard  
 CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, SK-842 16, Slovakia  
 SOURCE: Biomedical Chromatography (1997), 11(6), 348-351  
 CODEN: BICHR2; ISSN: 0269-3879  
 PUBLISHER: John Wiley & Sons Ltd.  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Simple one/two step purification procedures based on the solid-phase extraction technique were effectively exploited to clean up radiolabeled drugs represented by dihydrochloride of [6-3H]-stobadine and hydrochloride of [4-3H]-pentacaine, derivatization agents such as 4-nitrobenzoyl chloride or 3,5-dinitrobenzoyl chloride, as well as the aqueous phosphate or triethylamine acetate buffer solutions.  
 IT 85202-17-1p, (-)-Stobadine  
 RL: PUR (Purification or recovery); PREP (Preparation) (purification of various materials by solid-phase extraction)  
 RN 85202-17-1 CA  
 CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)-(9CI) (CA INDEX NAME)  
 Absolute stereochemistry. Rotation (-).

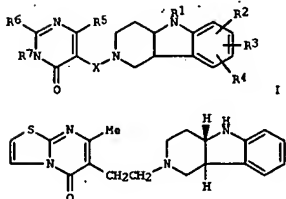


REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

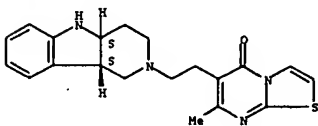
L9 ANSWER 40 OF 134 CA COPYRIGHT 2005 ACS ON STN  
 ACCESSION NUMBER: 128:34772 CA  
 TITLE: Hexahydropyrido[4,3-b]indole derivatives as antipsychotic drugs  
 INVENTOR(S): Kozma, Ludo Edmond Josephine; Martens, Josephus Carolus  
 PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.  
 SOURCE: PCT Int. Appl., 29 pp.  
 CODEN: P1XXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9744040	A1	19971127	WO 1997-EP2710	19970515 <--
W1. AL, AM, AU, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, LC, LK, LR, LT, LV, MD, MG, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, AM, AZ, XG, XZ, MD, RU, TJ, TM				
RW: KE, LS, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
TW 470745	B	20020101	TF 1997-86105765	19970501 <--
CA 2254755	AA	19971127	CA 1997-2254755	19970515 <--
AU 9729616	A1	19971209	AU 1997-29616	19970515 <--
AU 714113	B2	19991216		
EP 902684	A1	19990324	EP 1997-924014	19970515 <--
EP 902684	B1	20030409		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, FI				
CN 1219875	A	19990616	CN 1997-194873	19970515 <--
JP 20000510860	T2	20000822	JP 1997-541588	19970515 <--
CZ 287961	B6	20010314	CZ 1998-3774	19970515 <--
AT 236636	E	20030415	AT 1997-924014	19970515
PT 902684	T	20030829	PT 1997-924014	19970515
IL 127177	A1	20031031	IL 1997-127177	19970515
ES 2196332	T3	20031216	ES 1997-924014	19970515
PL 187345	B1	20040630	PL 1997-330079	19970515
ZA 9704770	A	19981123	ZA 1997-4470	19970522 <--
KR 2000005226	A	20000125	KR 1998-707913	19981002 <--
US 6057325	A	20000502	US 1998-180366	19981109 <--
NO 9805389	A	19990120	NO 1998-5389	19981119 <--
NO 311724	B1	20020114		
PRIORITY APPL. INFO.:			EP 1996-201450	A 19960523
OTHER SOURCE(S):			WO 1997-EP2710	W 19970515
GI				

L9 ANSWER 40 OF 134 CA COPYRIGHT 2005 ACS ON STN (Continued)

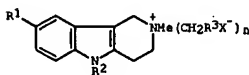


AB Title compds. I [X = alkanediyl; R1 = H, alkyl, aryl, aralkyl; R2, R3, R4 = H, halo, hydroxy, nitro, cyano, alkyl, alkoxy, trifluoromethyl, alkylthio, mercapto, amino, mono-, dialkylamino, carbonyl, alkylcarbonyl, alkylthio, (un)substituted NH2; R7 = H, alkyl; R6R7 = (un)substituted (CH2)3, (CH2)4, CH=CHCH2, CH2CH=CH, CH=CHCH=CH], having central dopamine and serotonin antagonistic activity, were prepared. Thus, 2-benzyl-2,3,4,5-tetrahydro-1H-pyrido[4,3-b]indole was reduced to the hexahydro analog, debenzylated, and treated with 6-(2-chloroethyl)-7-methyl-5H-thiazolo[3,2-a]pyrimidin-5-one to give the product II. II had dopamine and serotonin antagonistic activity in the combined apomorphine, tryptamine, and norepinephrine test in rats.  
 IT 199725-48-9p  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of hexahydropyrido[4,3-b]indole derivs. as antipsychotic drugs)  
 RN 199725-48-9 CA  
 CN 5H-Thiazolo[3,2-a]pyrimidin-5-one, 6-[2-(1,3,4,4a,5,9b-hexahydro-2H-pyrido[4,3-b]indol-2-yl)ethyl]-7-methyl-, trans- (9CI) (CA INDEX NAME)  
 Relative stereochemistry.



L9 ANSWER 41 OF 134 CA COPYRIGHT 2005 ACS ON STN  
 ACCESSION NUMBER: 127:248096 CA  
 TITLE: Preparation of hydrogenated pyrido[4,3-b]indole derivatives and pharmaceutical compositions and a method for treating neurodegenerative diseases  
 INVENTOR(S): Zefirov, Nikolai Serafimovich; Afanasiev, Andrei Zakharovich; Afanasieva, Svetlana Vasilievna; Bachurin, Sergei Olegovich; Thachenko, Sergei Evgenievich; Grigoriev, Vladimir Viktorovich; Jurovskaya, Marina Abramovna  
 PATENT ASSIGNEE(S): Isekuura Sangyo K. K., Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 156 pp.  
 CODEN: JXOXA  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

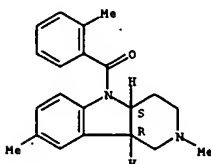
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 09216882	A2	19970819	JP 1996-274909	19961017 <--
RU 2140417	C1	19991027	RU 1995-117585	19951017 <--
PRIORITY APPL. INFO.:			RU 1995-117585	A 19951017
OTHER SOURCE(S):			MARPAT 127:248096	
GI				



AB The title derivs. I [dotted line represents an optional bond; R1 = H, lower alkyl; R2 = 2-[2-(N-methyl-N-3-methylamino)ethyl]-5-R1-indolyl-3-Me, (CH2)m(CHAlk)l(CH2)k [Y = H, halo, cycloalkyl, ethenyl which may be substituted with 1-3 lower alkyl, 1 aryl, CO2R4 at the 8-position (R4 = H, alkyl, aralkyl, aryl), OR4, alkylsulfonyl, arylsulfonyl, NR5R6 [R5 = H, alkyl, cycloalkyl, aralkyl, aryl, 2-, 3-, or 4-pyridyl, alkylsulfonyl, arylsulfonyl; one of R5 and R6 = COR7 (R7 = H, alkyl, alkoxy, cycloalkyl, aralkyl, aryl, 2-, 3-, or 4-pyridyl); or R5R6 = (CH2)2V(CH2)2 [V = O, (CH2)q (q = 0-2), N(CV)R8 (R8 = H, alkyl, aryl, CV = CH2, CO, C = 0-1)] or NR5R6 = N-phthalimido], OR9 (R9 = H, alkyl, aralkyl, aryl, OH, alkoxy, NR5R6 except N-phthalimido, 2-, 3-, or 4-pyridyl), cyano, CK3 (K = Cl, F, Br), aryl, 2-, 3-, or 4-pyridyl] or their quaternary ammonium salt, trialkylammonium, cycloalkylammonium, N-azinium, N-azolinium; CZ = CO, CS, CH2; k = 0-4; l, m, n = 0-1; R3 = (CH2)k' (Y' = any group given for Y); X = pharmcol. acceptable acid anion] and their pharmcol. acceptable salts are prepared by several methods. Also claimed are a method for treating diseases affecting glutamate neuromediator systems, e.g. neurodegenerative disorders, especially Alzheimer disease, with I and pharmaceutical compns. containing I.  
 2-Methyl-8-isopropyl-2,3,4,5-tetrahydro-1H-pyrido[4,3-b]indole hydrochloride (prepared from 4-isopropylphenylhydrazine hydrochloride and N-methyl-4-piperidone) showed ED50 17 mg/kg against convulsive death of mice induced by injection of NMDA into paracele. Pharmaceutical formulations containing I were also given.  
 IT 199326-87-5p

L9 ANSWER 41 OF 134 CA COPYRIGHT 2005 ACS on STN (Continued)  
 RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepn. of hydrogenated pyrdo[4,3-b]indole derivs. as NMDA antagonists for treating neurodegenerative diseases)  
 RN 195326-47-5 CA  
 CN 1H-Pyrdo[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-5-(2-methylbenzoyl)-, monohydrochloride, cis- (9CI) (CA INDEX NAME)

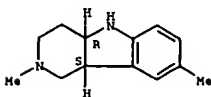
Relative stereochemistry.



• HCl

L9 ANSWER 43 OF 134 CA COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 126:325467 CA  
 TITLE: Mechanisms of hippocampal reoxygenation injury. Treatment with antioxidants  
 AUTHOR(S): Horakova, L.; Stolic, S.; Chromikova, Z.; Pekarova, A.; Derkova, L.  
 CORPORATE SOURCE: Inst. Experimental Pharmacol., Slovak Acad. Sci., Bratislava, 842 16, Slovakia  
 SOURCE: Neuropharmacology (1997), 36(2), 177-184  
 CODEN: NEUPHW; ISSN: 0028-3908  
 PUBLISHER: Elsevier  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The effects of hypoxia of different durations (8, 12 or 15 min) and of subsequent reoxygenation were studied in rat hippocampal slices by measuring enzyme activities related to oxidative stress: superoxide dismutase (SOD), cytochrome c oxidase and lactate dehydrogenase (LDH). Simultaneously the degree of lipid peroxidn. was estimated by measuring conjugated dienes (CD). Reoxygenation after 8-min of hypoxia induced general cell injury indicated by increased LDH activity. Reoxygenation after 12-min of hypoxia started lipid peroxidn. assessed by an increase in CD, and after 15-min of hypoxia followed by reoxygenation CD were found to be significantly decreased, suggesting lipid degradation. The injury induced by a hypoxia of 12 min and reoxygenation was reduced by SOD and catalase, indicating that oxygen radicals were involved in this process. The oxygen radicals originated from the xanthine/xanthine oxidase system, from the synthesis of prostaglandins, as well as from the mitochondrial respiratory chain, since allopurinol, indomethacin and rotenone decreased while antimycin increased reoxygenation injury. An increase in ATP may also have been involved as cyanide, an inhibitor of ATP synthesis, decreased the reoxygenation injury. The chain-breaking antioxidants trolox, alpha tocopherol and the pyridoindole stobadine were effective in preventing reoxygenation injury, indicating the involvement of lipid peroxidn. in this process.  
 IT 85202-17-1, Stobadine  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (mechanisms of hippocampal reoxygenation injury and treatment with antioxidants)  
 RN 85202-17-1 CA  
 CN 1H-Pyrdo[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)-(9CI) (CA INDEX NAME)

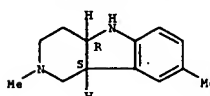
Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 42 OF 134 CA COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 127:158506 CA  
 TITLE: Stobadine pretreatment enhances glutathione peroxidase activity in the heart of irradiated mice  
 AUTHOR(S): Kovackikova, Zuzana; Chorvatovicova, Darina; Ginter, Eral  
 CORPORATE SOURCE: Institute of Preventive and Clinical Medicine, Bratislava, Slovakia  
 SOURCE: Methods and Findings in Experimental and Clinical Pharmacology (1997), 19(4), 241-243  
 CODEN: MFPEIX; ISSN: 0379-0355  
 PUBLISHER: Frous  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The effect of pretreatment with stobadine (a novel drug with cardioprotective properties) on the activity of glutathione peroxidase was studied in the heart of mice after Co60 irradiation. Exposure to 6.5 Gy caused significant decrease in the activity of the enzyme. Treatment with stobadine (70.07 mg/kg) 1 or 2 h before irradiation resulted in activity enhancement in comparison with the non-pretreated irradiated group. We conclude that the radical scavenging mechanism may be involved in the protection exerted by stobadine. The results are in agreement with those obtained by the micronucleus test.  
 IT 85202-17-1, Stobadine  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (stobadine pretreatment enhances glutathione peroxidase activity in the heart of irradiated mice)  
 RN 85202-17-1 CA  
 CN 1H-Pyrdo[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)-(9CI) (CA INDEX NAME)

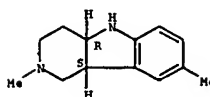
Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 44 OF 134 CA COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 126:271624 CA  
 TITLE: Neuroprotection by the pyridoindole stobadine: a minireview  
 AUTHOR(S): Stolic, S.; Vlkolinsky, R.; Pavlasek, J.  
 CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, SK-842 16, Slovakia  
 SOURCE: Brain Research Bulletin (1997), 42(5), 335-340  
 CODEN: BRBUDD; ISSN: 0361-9230  
 PUBLISHER: Elsevier  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB A review, with 55 refs., summarizing data documenting that stobadine (STB) may protect nerve structures against oxidative stress. This was demonstrated by the impairment of synaptic transmission in hippocampal slices and sympathetic ganglia exposed to hypoxia/reoxygenation (H/R) in vitro as well as by survival of rats and dogs exposed to brain ischemia/reperfusion (I/R) in vivo. The STB effect was linked mostly to its free-radical-scavenging and antioxidant properties. STB seems to act primarily on phospholipids, thus protecting the integrity and function of somatic membranes in neurons as well as those in subcellular organelles, such as mitochondria and endoplasmic reticulum. STB prevented damage to Ca2+-sequestering systems in endoplasmic reticulum and synaptosomes induced by lipid-peroxidn. initiators. STB diminished changes in NMDA and adrenergic α1-receptors evoked in the brain by I/R or H/R. It prevented the decrease in brain total thiols, participating in tissue antioxidant protection, under these conditions. It readily penetrates into both the hydrophilic and the hydrophobic compartments of the central nervous system. In I/R, protection of structures such as cerebral blood vessels, endothelium, and/or erythrocytes may participate in the effect of STB, besides the direct protection of nervous tissue. STB may be a potential protectant of the central nervous system in diseases in which oxidative injury may play an important role, i.e., stroke, neurotrauma, chronic brain ischemia, or some neurodegenerative diseases. It could provide a useful model in the further search for novel compds. with even more pertinent pharmacol. and pharmacokinetic profiles.  
 IT 85202-17-1, Stobadine  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (neuroprotection by)  
 RN 85202-17-1 CA  
 CN 1H-Pyrdo[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, (4aR,9bS)-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

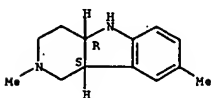


L9 ANSWER 45 OF 134 CA COPYRIGHT 2005 ACS ON STN  
 ACCESSION NUMBER: 126:233312 CA  
 TITLE: Effect of long-term administration of stobadine on exploratory behavior and on striatal levels of dopamine and serotonin in rats and their offspring  
 AUTHOR(S): Dubovický, M.; Ujhazy, E.; Kovacovsky, P.; Rychlik, I.; Kalnovicova, T.; Navarova, J.; Turcani, P.; Durisova, M.; Gajdosik, A.  
 CORPORATE SOURCE: Inst. Experimental Pharmacol., Bratislava, Slovakia  
 SOURCE: Journal of Applied Toxicology (1997), 17(1), 63-70  
 CODEN: JJATDK; ISSN: 0260-437X  
 PUBLISHER: Wiley  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Stobadine (STB), a cardioprotective drug, was evaluated for its effect on the intensity and habituation of exploratory behavior in open field testing and on the levels of striatal dopamine (DA), serotonin (5-HT) and their metabolites (3,4-dihydroxyphenylacetic acid, homovanillic acid, 5-hydroxyindole-3-acetic acid) in rats and their offspring. Dams were treated by oral gavage with STB (50 mg kg<sup>-1</sup>) for a total of 56 days from 14 days before mating to day 21 postpartum (pp). The first open field measurements of the dams were performed over 4 days at the beginning of the experiment, the second on days 21-24 pp and the third on days 49-52 (recovery period). Their offspring were tested on postnatal (pn) days 30-33 and 60-63. The biochem. anal. (HPLC with electrochem. detection) in the dams was performed at the same time schedule as given for the open field testing, but in their offspring only on pn day 60. Motor activity of the dams was decreased on days 21-24 pp. The increase of motor activity in female offspring was observed on pn days 30-33. Neurochem. anal. of the striatum of the dams revealed a significant increase of the levels of DA, 5-HT and 5-hydroxyindole-3-acetic acid. In male offspring the levels of DA were significantly decreased, whereas in females the levels were increased. These results suggest that maternal administration of STB resulted both in dams and their offspring in minor alterations in spontaneous behavior components and changes in the dopaminergic and serotonergic system, but without inducing overtly detectable toxicity.  
 IT 85202-18-2, BP 1031  
 RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (effect of long-term administration of stobadine on exploratory behavior and on striatal levels of dopamine and serotonin in rats and their offspring)  
 RN 85202-18-2 CA  
 CN Hexadecanoic acid, compd. with (4aR,9bS)-2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-1H-pyrido[4,3-b]indole (2:1) (9CI) (CA INDEX NAME)  
 CH 1  
 CRN 85202-17-1  
 CNF C13 H18 N2

Absolute stereochemistry. Rotation (-).

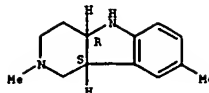
L9 ANSWER 46 OF 134 CA COPYRIGHT 2005 ACS ON STN  
 ACCESSION NUMBER: 126:796 CA  
 TITLE: Effect of long-term administration of stobadine to rats on selective variables of spontaneous behavior of their offspring  
 AUTHOR(S): Dubovický, M.; Kovacovsky, P.; Rychlik, I.; Ujhazy, E.; Gajdosik, A.  
 CORPORATE SOURCE: Institute Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, 82416, Slovakia  
 SOURCE: General Physiology and Biophysics (1996), 15(2), 181-186  
 CODEN: GPBIK2; ISSN: 0231-5882  
 PUBLISHER: Institute of Molecular Physiology and Genetics, Slovak Academy of Sciences  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB The present study investigated the effect of long-term administration of the cardioprotective drug stobadine (STB) to dams on selective variables of spontaneous behavior of their offspring in open field (horizontal and vertical activities, frequency and duration of grooming, and duration of total activity and immobility) tested on day 60 of age. The treatment of dams with STB significantly increased horizontal activity of offspring in both sexes. The other variables studied were not affected, with the exception of a significant increase in the frequency and duration of grooming and in the duration of total activity in females compared to males from STB treated dams.  
 IT 95751-51-2, Stobadine  
 RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
 (effect of long-term administration of stobadine to rats on selective variables of spontaneous behavior of their offspring)  
 RN 95751-51-2 CA  
 CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, dihydrochloride, (4aR,9bS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



● 2 HCl

L9 ANSWER 45 OF 134 CA COPYRIGHT 2005 ACS ON STN (Continued)



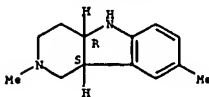
CH 2

CRN 57-10-3  
 CNF C16 H22 O2

HO<sub>2</sub>C-(CH<sub>2</sub>)<sub>14</sub>-Me

L9 ANSWER 47 OF 134 CA COPYRIGHT 2005 ACS ON STN  
 ACCESSION NUMBER: 125:185795 CA  
 TITLE: Transport of an antihypoxic drug stobadine across the blood-brain barrier in rat striatum and its influence on catecholamine-oxidative current: A voltammetric study under normal and anoxic/ischemic conditions  
 AUTHOR(S): Pavlasek, J.; Haburcak, M.; Masanova, C.; Stolic, S.  
 CORPORATE SOURCE: Institute Normal and Pathological Physiology, Slovak Academy of Sciences, Bratislava, Slovakia  
 SOURCE: Physiological Research (Prague) (1996), 45(3), 193-204  
 CODEN: PHSRJ; ISSN: 0862-8408  
 PUBLISHER: Academia  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Differential pulse voltammetry with a carbon fiber microelectrode (ME) was used in pentobarbital-anesthetized rats for monitoring the stobadine current (STB.C) on both sides of the blood-brain barrier (BBB) in the arterial bloodstream (BS) and in the corpus striatum (CS). The STB.C exhibited a distinct peak at a polarization voltage 540±30 mV. The maximum of STB.C in BS attained 2-3 min after the STB administration (2.8 mg/100 g in 1.0 ml saline solution i.a.) was followed by a rapid decrease to about 20% within next 3 min. The STB readily passed across the BBB: the STB.C peak appeared in the CS in the 3rd minute and continued to rise up to the 30th min. The administration of STB did not prevent a large increase (1347±326 %) of the catechol-oxidative current (CA.O.C) occurring in the CS between the 4th and 5th minute after cardiac arrest. However, a decrease of ME sensitivity to CA.O.C in the presence of STB was observed. This fact leads to the speculation whether a similar "quenching" of dopamine by STB could not participate in the protective effects of STB observed in the brain exposed to hypoxia-reoxygenation.  
 IT 95751-51-2, Stobadine  
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (transport of an antihypoxic drug stobadine across the blood-brain barrier in rat striatum and its influence on catecholamine-oxidative current)  
 RN 95751-51-2 CA  
 CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, dihydrochloride, (4aR,9bS)- (9CI) (CA INDEX NAME)

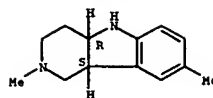
Absolute stereochemistry. Rotation (-).



● 2 HCl

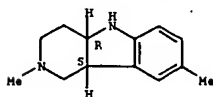
L9 ANSWER 48 OF 134 CA COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 125:76265 CA  
 TITLE: Rabbit brain endoplasmic reticulum membranes as target for free radicals. Changes in  $\text{Ca}^{2+}$ -transport and protection by stobadine  
 AUTHOR(S): Rasczy, Peter; Kaplan, Peter; Lehotsky, Jan; Mezesova, Viera  
 CORPORATE SOURCE: Comenius Univ., Dep. Biochem., Martin, SK-036 01, Slovakia  
 SOURCE: Biochemistry and Molecular Biology International (1995), 36(3), 569-577  
 CODEN: EMBIES; ISSN: 1039-9712  
 PUBLISHER: Academic  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB Incubation of rabbit brain endoplasmic reticulum membranes with either ferrous sulfate/EDTA or ferrous sulfate/KDTA and hydrogen peroxide led to the loss of efficiency of membranes to sequester  $\text{Ca}^{2+}$ , which did not correlate with changes in conjugated diene formation. The production of practically non-detectable amount of conjugated dienes that occurs during the period of incubation of microsomes with lipid peroxid. initiators represents lipid peroxid. that is enough to produce changes in membrane permeability towards  $\text{Ca}^{2+}$ . Addition of stobadine was able to prevent  $\text{Ca}^{2+}$  transport damage in a dose-dependent manner and drug concns. higher than 200  $\mu\text{M}$  were able in the authors model system to confer the defense against free radical and heavy metal initiated lipid peroxid. The EC50 values for microsomes with  $\text{Fe}^{2+}$  and  $\text{Fe}^{2+}/\text{H}_2\text{O}_2$  were 12  $\mu\text{M}$  and 25  $\mu\text{M}$ , resp. In the authors model system, stobadine seems to be at least as effective as butylated hydroxytoluene, which is considered to be a good chain-breaking antioxidant. In contrast to stobadine,  $\alpha$ -tocopherol acetate was less potent, the effect of 1 mM  $\alpha$ -tocopherol acetate being comparable to the effect of 20  $\mu\text{M}$  stobadine.  
 IT 95751-51-2, Stobadine  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (rabbit brain endoplasmic reticulum membranes as target for free radicals determined by lipid peroxid. in relation to changes in  $\text{Ca}^{2+}$ -transport and protection by antioxidant stobadine)  
 RN 95751-51-2 CA  
 CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, dihydrochloride, (4aR,9bS)- (9CI) (CA INDEX NAME)  
 Absolute stereochemistry. Rotation (-).

L9 ANSWER 48 OF 134 CA COPYRIGHT 2005 ACS on STN (Continued)



● 2 HCl

L9 ANSWER 49 OF 134 CA COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 125:3697 CA  
 TITLE: The pyridoindole antioxidant stobadine inhibited glycation-induced absorbance and fluorescence changes in albumin  
 AUTHOR(S): Stefek, M.; Drozdikova, I.; Vajdova, K.  
 CORPORATE SOURCE: Institute of Experimental Pharmacology, Slovak Academy of Sciences, Bratislava, 84216, Slovakia  
 SOURCE: Acta Diabetologica (1996), 33(1), 35-40  
 CODEN: ACDAEZ; ISSN: 0940-5429  
 PUBLISHER: Springer  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB We studied the effect of the pyridoindole antioxidant stobadine on glycation-induced absorbance and fluorescence changes in bovine serum albumin (BSA), used as a model protein. Incubation of BSA (4 mg/mL) with glucose (100-400 mM) in 0.12 M phosphate buffer, pH 7.4, in the presence of 100  $\mu\text{M}$   $\text{Cu}^{2+}$  at 37° resulted in a time-dependent increase of absorbance (320 nm) and fluorescence (excitation 350 nm, emission 415 nm). The process was found to be dependent on the presence of oxygen and transition metal ions, but equimolar iron could not fully substitute for the activity of copper. The glucose-induced chromo- and fluorophore formation was reduced significantly by stobadine. For 200  $\mu\text{M}$  glucose, in 7- and 14-day incubations, 51%-60% inhibition was obtained at a stobadine concentration of 0.1 mM, and the effect leveled off at higher concns. of the drug. No inhibition was observed with N-acetyl stobadine, a derivative with restricted antioxidant activity. Since stobadine did not affect the Amadori product formation determined by the thiobarbituric acid (TBA) method as 5-hydroxymethyl furfural (5-HMF) released in boiling oxalic acid, the inhibitory action of stobadine may be explained by its interference with metal-catalyzed oxidation reactions following after the glycation step. The results obtained suggest that antioxidant therapy could be used to limit the damage from adverse glycation-induced processes in diabetes mellitus.  
 IT 95751-51-2, Stobadine  
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)  
 (pyridoindole antioxidant stobadine inhibited glycation-induced absorbance and fluorescence changes in albumin)  
 RN 95751-51-2 CA  
 CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, dihydrochloride, (4aR,9bS)- (9CI) (CA INDEX NAME)  
 Absolute stereochemistry. Rotation (-).

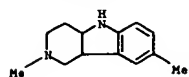


● 2 HCl

L9 ANSWER 50 OF 134 CA COPYRIGHT 2005 ACS on STN  
 ACCESSION NUMBER: 124:332651 CA  
 TITLE: Simultaneous monitoring of dopamine, its metabolites and trans-isomer of atypical neuroleptic drug carbide concentrations in striatal dialyzates of conscious rats  
 AUTHOR(S): Gainetdinov, Raul R.; Sotnikova, Tatyana D.; Grekhova, Tatyana V.; Rayevsky, Kirill S.  
 CORPORATE SOURCE: Institute Pharmacology, Russian Academy Medical Sciences, Moscow, Russia  
 SOURCE: Progress in Neuro-Psychopharmacology & Biological Psychiatry (1996), 20(2), 291-305  
 CODEN: PNPPD7; ISSN: 0276-5846  
 PUBLISHER: Elsevier  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 AB 1. Transcerebral microdialysis was used to monitor dopamine, 3,4-dihydroxyphenylacetic acid (DOPAC), homovanillic acid (HVA) and trans-isomer of atypical neuroleptic drug carbide concns. in the dialyzates from dorsal striatum of freely moving rats following i.p. administration of the drug at doses 0.5, 1, 5 and 25 mg/kg. The changes in locomotor activity as well as catalepsy in rats following trans-carbide administration were also evaluated. 2. The microdialysis "point of no net flux" method was used to measure interstitial free concentration (IPC) of trans-carbide in the dorsal striatum of freely moving rats following i.p. administration of the drug at dose 5 mg/kg. The maximal IPC of trans-carbide was found to be approx. 1  $\mu\text{M}$  20-40 min after injection. 3. The drug at doses up to 1 mg/kg produces elevation of dopamine release not affecting sufficiently its metabolite dialyzate levels. IPC of the drug calculated for these doses will not exceed 0.24  $\mu\text{M}$ . At the dose 5 mg/kg, i.p., elevation of both dopamine release and metabolism was observed and dopamine release increased slightly more than DOPAC dialyzate levels. 4. Stimulatory action of trans-carbide on locomotor activity of non-operated rats has been observed at doses 0.2 and 0.5 mg/kg, i.p. 5. Only the dose 25 mg/kg of trans-carbide (maximal calculated IPC 4.53  $\mu\text{M}$ ) was found to be cataleptogenic. The drug at this dose failed to increase DA release but induced a marked increase of DOPAC and HVA output. 6. It is concluded that trans-carbide in vivo neurochem. and behavioral studies demonstrates the preferential antagonistic action on dopamine release-regulating autoreceptors.  
 IT 33162-17-3, Carbide  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (simultaneous monitoring of dopamine, metabolites and trans-isomer of atypical neuroleptic drug carbide concns. in striatal dialyzates of conscious rats)  
 RN 33162-17-3 CA  
 CN 1H-Pyrido[4,3-b]indole, 2,3,4,4a,5,9b-hexahydro-2,8-dimethyl-, dihydrochloride (8CI, 9CI) (CA INDEX NAME)

10/743,449

L9 ANSWER 50 OF 134 CA COPYRIGHT 2005 ACS on STN (Continued)



● 2 HCl

10/743,449

=> d his

(FILE 'HOME' ENTERED AT 14:48:20 ON 13 JUL 2005)

FILE 'REGISTRY' ENTERED AT 14:48:25 ON 13 JUL 2005

L1 STRUCTURE UPLOADED

L2 42 S L1 SAM

L3 1026 S L1 FULL

FILE 'CA' ENTERED AT 14:49:03 ON 13 JUL 2005

L4 315 S L3

L5 2702 S 5HT

L6 1 S L4 AND L5

L7 149 S L4 AND (PHARM? OR DRUG?)

L8 150 S L6 OR L7

L9 134 S L7 AND PY<2003

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---Logging off of STN---

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Executing the logoff script...

=> LOG Y

STN INTERNATIONAL LOGOFF AT 14:50:42 ON 13 JUL 2005